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**PATENT APPLICATION  
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Box Patent Application

Transmitted herewith for filing is the patent application of

Inventor(s): **Jon THORSON**

For : **MICROMONOSPORA ECHNIOSPORA GENES ENCODING FOR  
BIOSYNTHESIS OF CALICHEAMICIN AND SELF-RESISTANCE  
THERE TO**

Enclosed are:

1. **51** sheets of specification, **16** sheets of claims, and **1** sheet of abstract.
2. **18** sheet(s) of drawings.
3. 127 sheets of sequence listing.
4. Related Application:

This application claims priority under 35 U.S.C. 120 of U.S. Patent Application Serial No. 09/457,045, filed December 7, 1999, which in turns claims priority under 35 U.S.C. 119(e) of provisional application No. 60/111,325, filed December 7, 1998.

5. Filing fees are not being paid at this time.

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***Micromonospora echinospora* genes encoding for biosynthesis of  
calicheamicin and self-resistance thereto**

This application is a continuation-in-part of the non-provisional application 09/457045, filed December 7, 1999 and claims benefit thereof, which application is incorporated herein by reference in its entirety. This application also claims benefit from provisional application 60/111,325 filed on December 7, 1998, which application is incorporated herein by reference in its entirety.

**Field of the Invention**

The present invention relates to a biosynthetic gene cluster of *Micromonospora echinospora* spp. *calichensis*. In particular, the calicheamicin biosynthetic gene cluster contains genes encoding for proteins and enzymes used in the biosynthetic pathway and construction of calicheamicin's aryltetrasaccharide and aglycone, and the gene conferring calicheamicin resistance. The present invention also relates to isolated genes of the biosynthetic cluster and their corresponding proteins. In addition, the invention relates to DNA hybridizing with the calicheamicin gene cluster and the isolated genes of that cluster. The invention also relates to expression vectors containing the biosynthetic gene cluster, the individual genes, or functional variants thereof.

**Background of the Invention**

The enediyne antibiotics, which were discovered in the 1980's, have long been appreciated for their novel molecular architecture, their remarkable biological activity, and their fascinating mode of action. Enediyne antibiotics were originally derived by

fermentation of microorganisms, including *Micromonospora*, *Actinomadura*, and *Streptomyces*. Rothstein, D. M., *Enediyne Antibiotics as Antitumor Agents*, p. 2 (1995). As a class, the enediyne antibiotics have been referred to as the most potent and highly active antitumor reagents yet discovered. Rothstein, D. M., *Enediyne Antibiotics as Antitumor Agents*, preface (1995).

To date, at least twelve members of this family of antibiotics have been discovered, all of which fall roughly into two categories. The members of the first category of enediynes are classified as chromoprotein enediynes because they possess a novel 9-membered ring chromophore core structure, which also requires a specific associated protein for chromophore stabilization. The members of the second category of enediyne are classified as non-chromoprotein enediynes. These enediynes contain a 10-membered ring, which requires no additional stabilization factors. This enediyne ring structure is often referred to as the "warhead." The warhead induces DNA damage, which is frequently a double-stranded cleavage and appears to be irreparable. This type of DNA damage is usually nonrepairable for the cell and is most often lethal. Because of these remarkable chemical and biological properties, there has been an intense effort by both the pharmaceutical industry and academia to study these substances with the goal of developing new and clinically useful therapeutic anti-tumor agents.

The 9-membered ring chromoprotein enediyne subfamily is comprised of: neocarzinostatin from *Streptomyces carzinostaticus*, (Myers, A.G., et al., *J. Am. Chem. Soc.*, 110, 7212-7214 (1988)); kedarcidin from *Actinomycete* L585-6, (Leet, J.E., et al., *J. Am. Chem. Soc.*, 114, 7946-7948 (1992)), N1999A2 from *Streptomyces globisporus*, (Yoshida, K., et al. *Tetrahedron Lett.*, 34, 2637-2640 (1993)), maduropeptin from

*Actinomadura madurea*, (Schroeder, D.R., et al., *J. Am. Chem. Soc.*, 116, 9351-9352 (1994)); N1999A2 from *Streptomyces* sp. AJ9493, (Schroeder, D.R., et al., *J. Am. Chem. Soc.*, 116, 9351-9352 (1994)); actinoxanthin from *Actinomyces globisporus*, (Khokhlov, A.S., et al., *J. Antibiot.*, XXII, 541-544 (1969)); largomycin from *Streptomyces pluricologrescens*, (Yamaguchi, T., et al., *J. Antibiot.*, XXIII, 369-372 (1970)); auromomycin from *Streptomyces macromomyceticus*, (Yamashita, T., et al., *J. Antibiot.*, XXXII, 330-339 (1979)), and sporamycin from *Streptosporangium pseudovulgare*, (Komiya, K., et al., *J. Antibiot.*, XXX, 202-208 (1977)), all of which are believed to possess a novel bicyclo[7.3.0.]dodecadiynene chromophore core structure essential for biological activity. In addition, with the exception of N1999A2, a required apoprotein acts as a stabilizer and specific carrier for the unstable chromophore, and for its transport and interaction with target DNA.

The non-chromophore enediynes subfamily is comprised of calicheamicin from *Micromonospora echinospora* spp. *calichensis*; namenamycin from *Polysyncraton lithostrotum*; esperamicin from *Actinomadura verrucosospora*; and dynemicin from *Micromonospora chersina*.

Enediynes antibiotics have potential as anticancer agents because of their ability to cleave DNA; however, many of these compounds are too toxic to be used currently in clinical studies. Today, only calicheamicin is known to be currently used in clinical trials; and it has provided promising results as an anticancer agent. For example, MyloTarg™, a calicheamicin-antibody conjugate also known as CMA-676 was approved by the FDA in January of 2000 to treat acute myelogenous leukemia. The enediynes also potentially have utility as anti-infective agents, provided that toxicity can be managed.



Calicheamicin has two distinct structural regions: the aryltetrasaccharide and the aglycone (also known as the warhead). The aryltetrasaccharide displays a highly unusual series of glycosidic, thioester, and hydroxylamine linkages and serves to deliver the drug primarily to specific tracts (5'-TCCT-3' and 5'-TTTT-3') within the minor groove of DNA when those sequences are available. However, specificity is also context-dependent. The aglycone of calicheamicin consists of a highly functionalized bicyclo[7.3.1]tridecadiynene core structure with an allylic trisulfide serving as the triggering mechanism. McGahren, W.J., et al., *Enediynes Antibiotics as Antitumor Agents*, pp. 75-86 (1995). Once the aryltetrasaccharide is firmly docked, aromatization of the bicyclo[7.3.1]tridecadiynene core structure, via a 1,4-dehydrobenzene-diradical, results in the site specific oxidative double strand scission of the targeted DNA. Zein, N., et al., *Science*, 240, 1198-1201 (1988). The aglycone undergoes a reaction that yields carbon-centered diradicals, which are responsible for DNA cleavage.

This activity of calicheamicin has sparked considerable interest in the pharmaceutical industry culminating in the recent FDA approval of the calicheamicin-antibody conjugate MyloTarg™ (CMA-676) to treat acute myelogenous leukemia (AML). Additionally, similar strategies have been used in phase I trials to treat breast cancer. A massive program to examine calicheamicin conjugated to alternative delivery systems has also recently been undertaken. Hamann, P.R., et al., *87th Annual Meeting of the American Association of Cancer Research*, Washington, D.C., pp. 471 (1996); Hinman, L.M., et al., *Cancer Res.*, 53, 3336 (1993); Hinman, L. M., et al., *Enediynes Antibiotics as Antitumor Agents*, pp. 87- 105 (1995); Sievers, E.L., et al., *Blood*, 93, 3678-3684 (1999); Siegel, M.M., et al., *Anal. Chem.*, 69, 2716-2726 (1997); Ellestad, G. personal communication.

The biological activity and molecular architecture of calicheamicin has also prompted a search for potentially useful analogs. Of the numerous laboratories producing synthetic analogs, one group has produced a novel calicheamicin  $\gamma^1$ , shown to effectively suppress growth and dissemination of liver metastases in a syngeneic model of murine neuroblastoma. Lode, H. N., et al., *Cancer Res.*, 58, 2925-2928 (1998); Wrasidlo, W., et al., *Acta Oncologica*, 34, 157-164 (1995). In addition to synthesizing calicheamicin analogs, random mutagenesis of *M. echinospora* and screening for mutant strains with improved biosynthetic potential has also been pursued. Rothstein, D. M., *Enediyne Antibiotics as Antitumor Agents*, pp. 107-126 (1995).

The first total synthesis of calicheamicin was reported by Nicolaou and coworkers in 1992. Synthesizing this complex antibiotic, though, presents many disadvantages. For example, Nacelle's procedure only provides approximately a 0.007% yield and requires 47 steps. Halcomb, R.L., *Enediyne Antibiotics as Antitumor Agents*, pp. 383-439 (1995). Thus, the total synthesis of calicheamicin remains secondary to the isolation of calicheamicin from large fermentations of *M. echinospora*. Therefore, methods to produce mass amounts of calicheamicin and potentially useful variants are still needed. Fantini, A., et al., *Enediyne Antibiotics as Antitumor Agents*, pp. 29-48 (1995). Transforming calicheamicin DNA into producing strains of bacteria, such as *Streptomyces*, *Micromonospora*, other actinomyces species, or *E. coli*, as non-limiting examples, would address this need. However, prior to the discoveries of the present inventors, no cloned *M. echinospora* genes were available, and only a set of limited studies upon putative *M. echinospora* promoters were available. Lin, L.S., et al., *J. Gen. Microbiol.*, 138, 1881-1885

(1992); Lin, L.S., et al., *J. Bacteriol.*, 174, 3111-3117 (1992); Baum, E.Z., et al., *J. Bacteriol.*, 171, 6503-6510 (1989); Baum, E.Z., et al., *J. Bacteriol.*, 170, 71-77 (1988).

Calicheamicin's molecular architecture in conjunction with its useful biological activity and potential therapeutic value brand calicheamicin an target for the study of natural product biosynthesis. While the radical-based mechanism of oxidative DNA cleavage by calicheamicin (i.e. aromatization of the bicyclo[7.3.1]tridecadiynene core structure, via a 1,4-dehydrobenzene-diradical, resulting in the site specific oxidative double strand DNA cleavage) is well understood, it was unknown, prior to this invention, how *Micromonospora* constructs calicheamicin. As a result, before the present invention, there was a need to discover and understand calicheamicin biosynthesis. Prior to this discovery of the present inventors, knowledge of genes encoding for nonchromoprotein enediyne biosynthesis was completely lacking.

The toxicity of the enediyne compounds, including calicheamicin, centers on the problem of directing the compound to the cleave only the DNA of interest, such as tumor cell DNA, and not the DNA of the host. Due to calicheamicin's powerful ability to cleave DNA, scientists have investigated the mechanism by which calicheamicin-producing organism protects itself against the DNA-cleaving activity of the molecule. Rothstein, D. M., *Enediyne Antibiotics as Antitumor Agents*, p. 77 (1995). Prior to this invention, knowledge of genes encoding for non-chromoprotein enediyne self resistance was completely lacking.

### **Summary of the Invention**

The present invention relates to the first identification, isolation, and cloning of a nonchromoprotein enediyne biosynthetic gene cluster and mapping and nucleotide

sequence analysis of the genes within the cluster. The invention provides the entire calicheamicin-biosynthetic cluster and biochemical studies of aryltetrasaccharide biosynthesis. Furthermore, the calicheamicin self-resistance gene and protein have been isolated, as have the genes and resulting enzymes for steps within the calicheamicin cascade. The invention also provides for construction of enediyne overproducing strains, for rational biosynthetic modification of bioactive secondary metabolites, for new drug leads, and for an enediyne combinatorial biosynthesis program.

The present invention provides an isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora* comprising said nucleic acid molecule, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a protein, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a biologically active fragment of a protein. The isolated nucleic acid molecule may be single- or double-stranded. As used herein, a nucleic acid molecule, polypeptide, or protein described as being "from" e.g., an organism or gene cluster, may have been isolated from such organism or gene cluster; alternatively, it may be a molecule which has been produced using synthetic, chemical, recombinant, or other such methods and comprise an amino acid or nucleotide sequence which may be isolated from such organism or gene cluster.

The present invention provides forty-eight genes, twenty-seven of which encode structural genes with the remainder encoding a variety of functions. The present invention is drawn to the following genes or nucleic acids: *calC* (SEQ ID No. 1), *calH* (SEQ ID No. 3), *calG* (SEQ ID No. 5), *calA* (SEQ ID No. 7), *calB* (SEQ ID No. 9), *calD* (SEQ ID No. 11), *calF* (SEQ ID No. 13), *calI* (SEQ ID No. 15), *calJ* (SEQ ID No. 17), *calK* (SEQ ID

No. 19), *calL* (SEQ ID No. 21), *calM* (SEQ ID No. 23), *calN* (SEQ ID No. 25), *calO* (SEQ ID No. 27), *calP* (SEQ ID No. 29), *calQ* (SEQ ID No. 31), *calR* (SEQ ID No. 33), *calS* (SEQ ID No. 35), *calT* (SEQ ID No. 37), *calU* (SEQ ID No. 39), *calV* (SEQ ID No. 41), *calW* (SEQ ID No. 43), *calX* (SEQ ID No. 45), *6MSAS* (SEQ ID No. 47), *ActI* (SEQ ID No. 49), *ActII* (SEQ ID No. 51), *ActIII* (SEQ ID No. 53), *orf1* (SEQ ID No. 55), *orf2* (SEQ ID No. 57), *orf3* (SEQ ID No. 59), *orf4* (SEQ ID No. 61), *orf5* (SEQ ID No. 63), *orf6* (SEQ ID No. 65), *orf7* (SEQ ID No. 67), *orf8* (SEQ ID No. 69), *orfI* (SEQ ID No. 71), *orfII* (SEQ ID No. 73), *orfIII* (SEQ ID No. 75), *orfIV* (SEQ ID No. 77), *orfV* (SEQ ID No. 79), *orfVI* (SEQ ID No. 81), *orfVII* (SEQ ID No. 83), *orfVIII* (SEQ ID No. 85), *orfIX* (SEQ ID No. 87), *orfX* (SEQ ID No. 89), *orfXI* (SEQ ID No. 91), *IS-element* (DNA) (SEQ ID No. 93), *calE* (SEQ ID No. 94). The invention is also drawn to the following proteins or putative proteins: CalC (SEQ ID No. 2), CalH (SEQ ID No. 4), CalG (SEQ ID No. 6), CalA (SEQ ID No. 8), CalB (SEQ ID No. 10), CalD (SEQ ID No. 12), CalF (SEQ ID No. 14), CalI (SEQ ID No. 16), CalJ (SEQ ID No. 18), CalK (SEQ ID No. 20), CalL (SEQ ID No. 22), CalM (SEQ ID No. 24), CalN (SEQ ID No. 26), CalO (SEQ ID No. 28), CalP (SEQ ID No. 30), CalQ (SEQ ID No. 32), CalR (SEQ ID No. 34), CalS (SEQ ID No. 36), CalT (SEQ ID No. 38), CalU (SEQ ID No. 40), CalV (SEQ ID No. 42), CalW (SEQ ID No. 44), CalX (SEQ ID No. 46), *6MSAS* (SEQ ID No. 48), *ActI* (SEQ ID No. 50), *ActII* (SEQ ID No. 52), *ActIII* (SEQ ID No. 54), *Orf1* (SEQ ID No. 56), *Orf2* (SEQ ID No. 58), *Orf3* (SEQ ID No. 60), *Orf4* (SEQ ID No. 62), *Orf5* (SEQ ID No. 64), *Orf6* (SEQ ID No. 66), *Orf7* (SEQ ID No. 68), *Orf8* (SEQ ID No. 70), *OrfI* (SEQ ID No. 72), *OrfII* (SEQ ID No. 74), *OrfIII* (SEQ ID No. 76), *OrfIV* (SEQ ID No. 78), *OrfV* (SEQ ID No. 80), *OrfVI*

(SEQ ID No. 82), OrfVII (SEQ ID No. 84), OrfVIII (SEQ ID No. 86), OrfIX (SEQ ID No. 88), OrfX (SEQ ID No. 90), OrfXI (SEQ ID No. 92), CalE (SEQ ID No. 95).

In one aspect, the present invention is directed to an isolated nucleotide molecule, wherein the nucleotide molecule hybridizes with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94, or a functional derivative of the isolated nucleotide molecule which hybridizes with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94. In one embodiment of the invention, the isolated nucleotide molecule has the nucleotide sequence of at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94, i.e., 100% complementarity (sequence identity) with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94. In another embodiment of the invention, the isolated nucleotide molecule has at least 90% complementarity (sequence identity) with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94. In yet another embodiment of the invention, the isolated nucleotide molecule has at least 80% complementarity (sequence identity) with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89,

91, 93 or 94. In yet another embodiment of the invention, the isolated nucleotide molecule has at least 70% complementarity (sequence identity) with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94. In yet another embodiment of the invention, the isolated nucleotide molecule has at least 60% complementarity (sequence identity) with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94. In still yet another embodiment of the invention, the isolated nucleotide molecule is substantially complementary to at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94.

In another embodiment of the invention, there is provided an isolated protein encoded by a DNA molecule as described herein above, or a functional derivative thereof. A preferred protein has the amino acid sequence of at least one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95 or a functional variant or derivative of one or more of those polypeptides.

In another embodiment, the present invention provides an isolated nucleic acid molecule from *Micromonospora echinospora* comprising a nonchromoprotein enediyne biosynthetic gene cluster, a portion or portions of said gene cluster wherein said portion or portions encode a protein, a portion or portions of said gene cluster wherein said portion or portions encode a biologically active fragment of a protein, a single-stranded nucleic

acid molecule derived from said gene cluster, or a single-stranded nucleic acid molecule derived from a portion or portions of said gene cluster.

In particular, the present invention provides an isolated nucleic acid molecule from *Micromonospora echinospora* spp. *calichensis* that is involved in the biosynthesis of calicheamicin. In another embodiment, the present invention also relates to nucleic acids capable of hybridizing with one or more isolated nucleic acids from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora* spp. *calichensis*. In a further embodiment, the invention provides an expression vector comprising an isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora*. In yet a further embodiment the invention provides a cosmid comprising an isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora*.

In preferred embodiments, the invention provides the isolated nucleic acid molecules of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 and 94.

In an additional embodiment, the present invention provides a host cell transformed with an isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora*. Host cells can optionally be of bacterial, yeast, fungal, insect, plant or mammalian origin and can be transformed according to standard methods. In a preferred embodiment, the host cell is the bacterium *E. coli*, *Streptomyces* spp., or *Micromonospora* spp. In a more preferred embodiment, the host cell is the bacterium from the genus *Streptomyces* or from the genus *Micromonospora*.



In a further embodiment, the invention is directed to a host cell transformed with an expression vector comprising at least one of the nucleotide sequences of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, or 94 or a portion of portions thereof or an allele or alleles thereof. In preferred embodiments, the host cells produce a biologically functional protein or portion of a protein, which protein or portion thereof is encoded by the expression vector.

In a specific embodiment, the invention is directed to a host cell transformed with an expression vector comprising *calC*, or a portion(s) or allele(s) thereof, operably linked to regulatory sequences that enable expression of CalC. In another specific embodiment, the invention provides a host cell transformed with an expression vector comprising *calH*, or a portion(s) or allele(s) thereof, operably linked to regulatory sequences that enable expression of CalH. In a yet further specific embodiment, the invention provides a host cell transformed with an expression vector comprising *calQ*, or a portion(s) or allele(s) thereof, operably linked to regulatory sequences that enable expression of CalQ. Likewise, the invention provides a host cell transformed with an expression vector comprising *calG*, or a portion(s) or allele(s) thereof, operably linked to regulatory sequences that enable expression of CalG.

In a yet further embodiment, the invention is directed to a host cell transformed with an expression vector encoding at least one polypeptide comprising the amino acid sequence of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95 or a functional variant of one or more of those polypeptides. In

preferred embodiments, the host cells produce a biologically functional protein or portion of a protein, which protein or portion thereof is encoded by the expression vector.

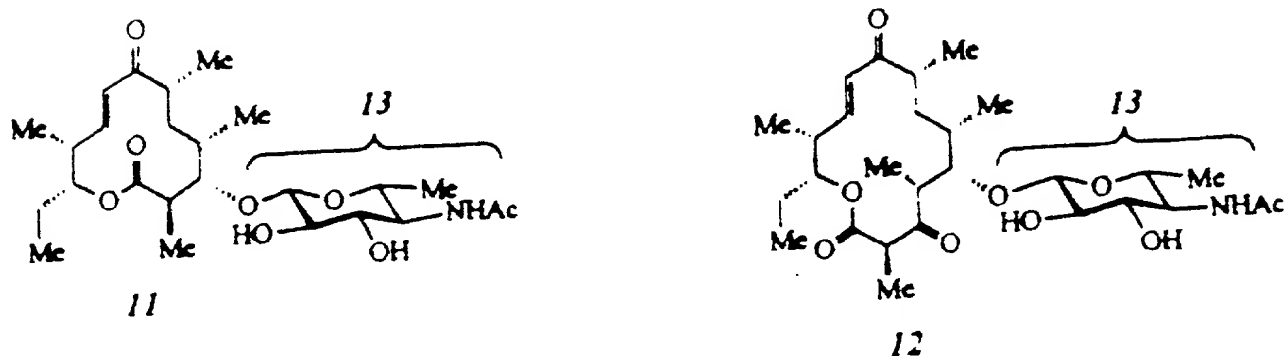
In a specific embodiment, the invention is directed to a host cell transformed with an expression vector encoding CalC, or a functional derivative thereof, operably linked to regulatory sequences that enable expression the encoded polypeptide. In another specific embodiment, the invention provides a host cell transformed with an expression vector encoding CalH, or a functional derivative thereof, operably linked to regulatory sequences that enable expression of the encoded polypeptide. In a yet another specific embodiment, the invention provides a host cell transformed with an expression vector encoding CalQ, or a functional derivative thereof, operably linked to regulatory sequences that enable expression of the encoded polypeptide. Likewise, the invention provides a host cell transformed with an expression vector encoding the CalG, or a functional derivative thereof, operably linked to regulatory sequences that enable expression of the encoded polypeptide.

The invention further provides a method of expressing a protein by culturing a host cell transformed with an expression vector of the present invention, and incubating the host cell for a time and under conditions allowing for protein expression.

In yet another embodiment the invention provides a method of purifying calicheamicin using affinity chromatography. A sample containing calicheamicin is contacted with an affinity matrix having the protein CalC bound thereto, for a time and under conditions allowing calicheamicin to bind to the matrix, eluting calicheamicin from the matrix, and recovering calicheamicin.

In a further embodiment the present invention provides polypeptides comprising the amino acid sequences of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 and 95.

In yet a further embodiment the invention provides the production of the following two new macrolides:



The invention further provides a method of conferring calicheamicin resistance to a subject comprising obtaining cells from the subject, transforming the cells with the calicheamicin self-resistance gene, and returning the cells to the subject. Alternatively, the calicheamicin self-resistance gene can be targeted and delivered to the desired host cells through known gene therapy delivery systems.

The invention further provides a method of producing calicheamicin analogs by altering calicheamicin or its bioactive metabolites through the modulation of the expression of *calD*, *E*, *F*, *G*, *H*, *J*, *K*, *N*, *O*, *P*, *Q*, *S*, *T*, *U*, *V*, *W*, *X*, *6MSAS*, *actI-III*, *orfI*, *orfIII*, *orfV*, and *orfVII*. Such modulation can be achieved through selective “knock out”,

as well as heterologous expression of these genes and their products. Various combinations of these either mutated or wild type gene products may be used in either *in vitro* or *in vivo* calicheamicin analog production.

The invention further provides a method for increasing the production of calicheamicin through the introduction of multiple copies of positive regulators and transporters and or by eliminating or reducing the expression of negative regulators (e.g., CalA, B, I, L, Orf8). Additionally, upregulation of calicheamicin resistance genes *calC*, *calN* and *orfXI* can be used to decrease the toxicity of calicheamicin to healthy tissues and cells during therapy.

In a yet further embodiment, the invention provides for a method of transposon mediated mutagenesis or moving chromosomal DNA fragments *in vivo* through expression of the *orf3* integrase and the IS insertional element.

The advantages of the present invention are numerous. Isolation of and the ability to clone calicheamicin DNA opens the door for genetic analysis of calicheamicin biosynthesis, as such analysis requires the ability to obtain large quantities of DNA which codes for calicheamicin biosynthesis. Using the teachings of the present invention, one can study calicheamicin biosynthesis via mutagenesis of *M. echinospora*. For example, one can isolate and characterize mutants blocked in calicheamicin biosynthesis and then analyze their defective or partial calicheamicin products. Additionally, particular a enzyme or enzymes can be overexpressed or underexpressed after subcloning its gene into a host such as *E. coli*, and the results of such overexpression or underexpression can be studied to reveal the enzyme's function. Furthermore, the cloning of biosynthetic genes

can ultimately result in increased yields of the gene product by cloning and expressing the biosynthetic gene encoding the rate-limiting enzyme back into the producing organism.

Further, it may also be possible to generate novel products by cloning biosynthetic genes into strains that make related compounds. Such genes could endow the host organism with the ability to carry out new reactions on the enediyne nucleus, and thus produce novel drugs. The present invention thus also provides means for biosynthetic modification of bioactive secondary metabolites through enediyne combinatorial biosynthesis. As most pharmaceutical drug leads are inspired by naturally occurring compounds, and given the challenge posed in synthesizing these metabolites, genetic manipulation of the sugar appendage on the metabolites offers avenues for creating potential new drugs. Thus the emerging field of combinatorial biosynthesis has become a rich new source for modified non-natural sugar scaffolds. Marsden, A., et al., *Science* 1998, 279, 199-201. Problems inherent with the genetic manipulation of the sugar appendage relate to the fact that naturally occurring bioactive secondary metabolites possess unusual carbohydrate ligands, which serve as molecular recognition elements critical for biological activity. *Macrolide Antibiotics, Chemistry, Biology and Practice*, 1984. Without these essential sugar attachments, the biological activities of most clinically important secondary metabolites are either completely abolished or dramatically decreased. Currently, techniques for the genetic manipulation of the sugar appendage for a given metabolite rely mainly on the alteration and/or deletion of a small subset of genes required to construct and attach each desired sugar moiety. Thus there is a need to develop alternate strategies to construct and attach non-naturally occurring sugars. The present invention addresses this need. The present invention utilizes the fact that

glycosyltransferases, which are responsible for the final glycosylation of certain secondary metabolites, show a high degree of promiscuity toward the nucleotide sugar donor. Zhao, L., et al., *J. Am. Chem. Soc.* 1988, 120, 12159-12160. This unselectivity of the glycosyltransferases has the potential for allowing modification of the crucial glycosylation pattern of natural, or non-natural, secondary metabolite scaffolds in a combinatorial fashion. The present invention discloses a method using the recruitment and collaborative action of sugar genes from a variety of biosynthetic pathways to construct composite gene clusters, which make and attach non-natural sugars.

Insight into how *Micromonospora* self resistance gene and gene products act to control the toxic effects of calicheamicin offers new avenues of clinical research. For example, knowledge of the mechanisms underlying calicheamicin resistance, as provided by the present disclosure, can provide the means necessary to use higher doses of calicheamicin while simultaneously inhibiting the toxic effects of the drug on non-cancer cells. Additionally, understanding the mechanism behind calicheamicin's self-resistance may aid in the understanding of self-resistance in other enediynes antibiotics, thereby potentially making useful those enediynes once thought to be too toxic to be viably used as therapeutic agents. The calicheamicin self-resistance mechanisms elucidated utilizing the present invention provide gene therapy approaches, for example, via introduction of enediynes resistance genes into bone marrow cells, thereby increasing resistance and allowing tolerance to chemotherapeutic doses of calicheamicin. Banerjee, D., et al., *Stem Cells*, 12, 378-385 (1994). Thus, understanding calicheamicin self-resistance will significantly aid continuing clinical studies involving calicheamicin and the enediynes. The present invention addresses this need as it provides for the isolation and

characterization of a resistance gene and its associated protein for any nonchromoprotein enediynes.

### Brief Description of the Figures

Figure 1 depicts the summary of the cosmid clones isolated from *M. echinospora* genomic library. This figure illustrates the results of the screening of the genomic library for clones carrying the calicheamicin biosynthetic cluster.

Figure 2 shows a restriction map of a portion of cosmid clones 4b, 13a, and 56 and the corresponding location of *cal* genes from *M. echinospora*.

Figure 3 is a table of the open reading frames ("orfs") in the calicheamicin biosynthetic cluster. This table lists the polypeptides that the genes encode for as well as their proposed or actual determined function in the biosynthetic pathway. <sup>a</sup> Assignments based upon BLAST search at the amino acid level unless otherwise noted. <sup>b</sup> Highest probability score obtained. <sup>c</sup> Assignment based on biochemical studies. <sup>d</sup> Only a portion of the orf has been elucidated.

Figure 4 is a graph of the UV-visible absorption spectra of purified mbp-CalC. The purified mbp-CalC was analyzed in the following solution: 52  $\mu$ M mbp-CalC; 10 mM Tris-HCl, pH 7.5). The inset shows the results of low temperature (4.3 K) the X-band EPR analysis of CalC. 250  $\mu$ M mbp-CalC containing 0.5 mol Fe per mol CalC was analyzed in 10 mM Tris-HCl, pH 7.5. The spectrometer settings were as follows: field set = 2050 G; scan range = 4,000G; time constant = 82 s; modulation amplitude = 16 G; microwave power = 31  $\mu$ W; frequency = 9.71 Ghz; gain = 1000; determined spin quantitation =  $90 \pm 10$   $\mu$ M Fe.

Figure 4(b) provides the results of the mbp-CalC *in vitro* assay.

Figure 5 depicts the postulated routes for the biosynthesis of required nucleotide sugars. The enzymes are depicted as follows:  $E_{\text{deox}}$  = deoxygenase;  $E_{\text{am}}$  = aminotransferase;  $E_{\text{ep}}$  = epimerase;  $E_{\text{met}}$  = methyltransferase;  $E_{\text{od}}$  = 4,6-dehydratase;  $E_{\text{ox}}$  = oxidase;  $E_{\text{p}}$  = nucleotidyltransferase;  $E_{\text{red}}$  = reductase;  $E_{\text{sh}}$  = sulfhydryltransferase.

Figure 6 illustrates a schematic representation of the *in vivo* production of pikromycin/methymycin-calicheamicin hybrid metabolites.

Figure 7 depicts the *Streptomyces venezuela* methymycin/pikromycin gene cluster. Eight open reading frames (*desI-desVIII*) in this cluster have been assigned as genes involved in desosamine biosynthesis. This figure also depicts the hybrid pathway toward new methymycin/pikromycin derivatives (11 and 12) produced after heterologous expression of the *calH* gene of calicheamicin in a *S. venezuela* mutant.

Figure 8 illustrates calicheamicin's (6) four unique sugars which are crucial to tight DNA binding. Sugar (9) is derived from 4-amino-4,6-dideoxyglucose (8) and is part of the restricted N-O connection between sugars A and B. Compound 8 is derived from the corresponding 4-ketosugar (7) via a transamination reaction. The gene *calH* encodes the desired C-4 aminotransferase allowing conversion of compound (7) to compound (8).

Figure 9 is a map illustrating the relative loci of the 48 identified genes spanning approximately 65KB of continuous sequence. Eight of the genes identified show no homologs in the public databases.

Figure 10 depicts additional postulated routes for the biosynthesis of required nucleotide sugars. The enzymes are depicted as follows:  $E_{\text{deox}}$  = deoxygenase;  $E_{\text{am}}$  = aminotransferase;  $E_{\text{ep}}$  = epimerase;  $E_{\text{met}}$  = methyltransferase;  $E_{\text{od}}$  = 4,6-dehydratase;  $E_{\text{ox}}$  = oxidase;  $E_{\text{p}}$  = nucleotidyltransferase;  $E_{\text{red}}$  = reductase;  $E_{\text{sh}}$  = sulfhydryltransferase.



Figure 11 is a schematic showing the iodination of orsellenic acid mediated by CalV and CalT, as well as the subsequent steps of oxidation, mediated by CalS and CalW and methylation, mediated by CalD and CalJ. Additionally, the figure shows the synthesis of putative substrates for the reaction.

Figure 12 describes the mechanism of calicheamicin resistance in *Micromonospora*. *calC* confers calicheamicin resistance to bacteria.

Figure 13 A schematic diagram of the first continuous assay for enediynes-induced DNA cleavage, the Molecular Break Lights. The solid lines represent covalent bonds, dashed lines represent hydrogen bonding, letters represent arbitrary bases, the gray shaded ball represents the fluorophore (FAM: fluorescein), the black ball represents the corresponding quencher (DABCYL:4-(4'-demethylaminophenylazo)-benzoic acid) and the dashed wedges represent fluorescence. Generally, molecular beacons operate by a separation of the fluorophore-quencher pair resulting in a corresponding fluorescent signal. Molecular break lights, as illustrated in the figure, operate through cleavage of the stem by an enzymatic or non-enzymatic nuclease activity resulting in the separation of the fluorophore-quencher pair and corresponding fluorescent signal. In this study, Molecular break lights contain either a preferred calicheamicin recognition site (bold-faced, TCCT) or the *Bam*HI recognition site (bold-faced, GGATCC). The predicted cleavage sites are illustrated by arrows.

Figure 14 shows the demonstration of molecular break light specificity and general proof of principle. The observed change in fluorescence intensity over time of an assay containing 3.2 nM break light at 37 °C. (a) Break light calicheamicin MLB (break light A) with 100 U *Bam*HI (□), *Bam*HI MLB (break light B) with 100 U *Bam*HI (○) and

*Bam*HI MLB without enzyme (•) (10 mM Tris HCl, 50 mM NaCl, 10 mM MgCl<sub>2</sub>, 1 mM DTT, pH 7.9;  $\lambda_{\text{Ex}} = 485 \text{ nm}$ ,  $\lambda_{\text{Em}} = 517 \text{ nm}$ ). (b) calicheamicin MLB (break light A) with and 10 U DNaseI (□), *Bam*HI MLB (break light B) with 10 U DNaseI (o) and calicheamicin MLB (break light A) without enzyme (•) (40 mM Tris HCl, 10 mM MgSO<sub>4</sub>, 1 mM CaCl<sub>2</sub>, pH 8.0;  $\lambda_{\text{Ex}} = 485 \text{ nm}$ ,  $\lambda_{\text{Em}} = 517 \text{ nm}$ ). This is the most sensitive assay for *Bam*HI and DNaseI DNA cleavage activity to date.

Figure 15 shows the cleavage of calicheamicin MLB (break light A) by calicheamicin and esperamicin. The observed DNA cleavage over time of an assay containing 3.2 calicheamicin MLB at 37 °C (40 mM Tris HCl, pH 7.5;  $\lambda_{\text{Ex}} = 485 \text{ nm}$ ,  $\lambda_{\text{Em}} = 517 \text{ nm}$ ), DTT (50  $\mu\text{M}$ ) and varied enediyne. (a) Calicheamicin concentrations: 31.7 nM (o), 15.9 nM (□), 3.2 nM (◇), 1.6 nM (Δ), 0.78 nM (•) and 0.31 nM (■). (b) Esperamicin concentrations: 31.7 nM (o), 15.9 nM (□), 3.2 nM (◇), 1.6 nM (Δ), 0.78 nM (•), 0.31 nM (■) and 0.15 nM (◆). These results represent the first continuous and most sensitive assay for enediyne-induced DNA cleavage.

Figure 16 (a) The observed DNA cleavage over time of an assay containing a constant 3.2 nM break light A at 37 °C (50 mM sodium phosphate, 2.5 mM ascorbate, pH 7.5;  $\lambda_{\text{Ex}} = 485 \text{ nm}$ ,  $\lambda_{\text{Em}} = 517 \text{ nm}$ ) and varied bleomycin. Bleomycin concentrations: 200 nM (o), 100 nM ( ), 50 nM (◇), 25 nM (Δ), 12.5 nM (•), 5 nM (■) and 2.5 nM (▲). (c) The observed DNA cleavage over time of an assay containing a constant 32 nM break light A at 37 °C (40 mM Tris HCl, 2.5 mM ascorbate, pH 7.5;  $\lambda_{\text{Ex}} = 485 \text{ nm}$ ,  $\lambda_{\text{Em}} = 517 \text{ nm}$ ) and varied MPE. Fe(II) concentrations: 50 nM (○), 125 nM (□), 250 nM (◇), 500 nM (Δ), 1  $\mu\text{M}$  (•) and 2  $\mu\text{M}$  (■). (d) The observed DNA cleavage over

time of an assay containing a constant 32 nM break light A at 37 °C (40 mM Tris HCl, 2.5 mM ascorbate, pH 7.5;  $\lambda_{\text{ex}}$  = 485 nm,  $\lambda_{\text{em}}$  = 517 nm) and varied Fe<sup>2+</sup>-EDTA. Fe(II) concentrations: 12.5  $\mu$ M (○), 6.3  $\mu$ M (□), 3.1  $\mu$ M (◇), and 1.3  $\mu$ M (Δ).

Figure 17 shows the direct in vitro inhibition of calicheamicin-mediated DNA cleavage using the break light assay. 3.6pM break light A is coincubated with 3.5nM calicheamicin with increasing amounts of CalC. Complete inhibition of calicheamicin is achieved with roughly 2-fold excess of CalC. CalC has no effect on esperamicin-induced cleavage of DNA.

Figure 18 shows the interaction between CalC and “activated” calicheamicin as measured by an increase in tryptophan fluorescence of CalC. CalC has 5 tryptophan and no cysteine residues and is unaffected by the reductive activator dithiothreitol (DTT). As the concentration of calicheamicin (3) increases in the absence of DTT there is little change in the CalC Trp fluorescence intensity. The addition of DTT to “activate” calicheamicin (4) results in increased binding to CalC as shown by the increase in CalC Trp fluorescence intensity.

### Detailed Description of the Invention

The present invention is directed to the isolation and characterization of the calicheamicin biosynthetic cluster. This cluster encodes the genes that encode the proteins and enzymes that are involved in deoxysugar synthesis (the aryltetrasaccharide), polyketide biosynthesis (the aglycone and aromatic residue of the aryltetrasaccharide) of calicheamicin synthesis, regulation, transport, cluster mobility and calicheamicin resistance. Forty-eight putative genes have been identified, twenty-seven of which encode

putative structural proteins with the remainder encoding a variety of functions.

Specifically, there are 15 genes that encode for the aryltetrasaccharide moiety (20,928 bp; *D, E, F, G, H, J, K, N, O, Q, S, T, U, X, W, 6MSAS*), 12 putative genes which encode for the aglycone (13,284 bp; *P, S, V, W, ActI, ActII, ActIII, OrfI, OrfIII, OrfV, OrfVI, OrfVII*), 13 putative genes involved in membrane transport, regulation, DNA movement and/or resistance (19,704 bp; *A, B, C, I, L, M, R, orf4, orf8, OrfVIII, OrfIX, OrfX, OrfXI, IS-element*), and the remaining 8 genes of unknown function (7383 bp; *orf1, orf2, orf3, orf5, orf6, orf7, OrfII, OrfIV*).

The calicheamicin biosynthetic gene cluster comprises the following genes: *calA, calB, calC, calD, calE, calF, calG, calH, calI, calJ, calK, calL, calM, calN, calO, calP, calQ, calR, calS, calT, calU, calV, calW, calX, 6MSAS, ActI, ActII, ActIII, orf1, orf2, orf3, orf4, orf5, orf6, orf7, orf8, orfI, orfII, orfIII, orfIV, orfV, orfVI, orfVII, orfVIII, orfIX, orfX, orfXI* and an IS-element gene. It should be noted that orf1-8 may contain DNA derived in whole or in part from recombinant vectors LP46 and/or LP54. The above listed genes encode the following polypeptides: CalA (328 amino acids), CalB (561 amino acids), CalC (181 amino acids), CalD (263 amino acids), CalE (420 amino acids), CalF (245 amino acids), CalG (990 amino acids), CalH (338 amino acids), CalI (568 amino acids), CalJ (332 amino acids), CalK (440 amino acids), Cal L (562 amino acids), Cal M (416 amino acids), CalN (398 amino acids), CalO (331 amino acids), Cal P (approximately 179 amino acids), CalQ (453 amino acids), CalR (265 amino acids), CalS (1113 amino acids), CalT (280 amino acids), CalU (377 amino acids), CalV (125 amino acids), CalW (449 amino acids), CalX (197 amino acids), 6MSAS (198 amino acids), ActI (207 amino acids), ActII (136 amino acids), ActIII (308 amino acids), OrfI(322 amino acids), Orf2

(654 amino acids), Orf3 (209 amino acids), Orf4 (521 amino acids), Orf5 (175 amino acids), Orf6 (139 amino acids), Orf7 (187 amino acids), Orf8 (266 amino acids), OrfI (127 amino acids), OrfII (248 amino acids), OrfIII (298 amino acids), OrfIV (363 amino acids), OrfV (288 amino acids), OrfVI (1012 amino acids), OrfVII (236 amino acids), OrfVIII (441 amino acids), OrfIX (504 amino acids), OrfX (504 amino acids), OrfXI (251 amino acids) and IS-element (402 amino acids).

In elucidating the calicheamicin biosynthetic gene cluster, the inventors began with a genomic library containing the genome of *Micromonospora echinospora* spp. *calichensis*. The cosmid library was generated by isolating chromosomal DNA of *Micromonospora echinospora* spp. *calichensis*, fragmenting that chromosomal DNA, inserting the DNA into a cosmid vector and generating a cosmid library according to methods well known in the art. This procedure can be performed using any species of *Micromonospora*, *Streptomyces*, or other suitable bacteria.

Based upon prior enediyne metabolic labeling studies it was postulated that the calicheamicin aglycone would be polyketide derived. Polyketide metabolites encompass a vast variety of structural diversities yet share a common mechanism of biosynthesis. Hutchinson, C.R., et al., *Chem. Rev.*, 97, 2525-2535 (1997); Strohl, W.R., et al., *Biotechnology of Antibiotics* pp. 577-657; Fujii, I., et al., *Chem. Rev.*, 97, 2511-2523 (1997); Hopwood, D.A., et al., *Chem. Rev.*, 97, 2465-2497 (1997); Hopwood, D.A., et al., *Ann. Rev. Genet.*, 24, 37-66 (1990); Staunton, J., et al., *Chemical Reviews*, 97, 2611-2629 (1997). Most important, polyketide synthase ("PKS") genes display a high degree of sequence homology (from pathway to pathway and organism to organism) and are often clustered with genes encoding self resistance and deoxysugar ligand biosynthesis.

Hopwood, D.A., et al., *Chem. Rev.*, 97, 2465-2497 (1997); Hopwood, D.A., et al., *Ann. Rev. Genet.*, 24, 37-66 (1990); Staunton, J., et al., *Chem. Rev.*, 97, 2611-2629 (1997).

Degenerate primers based upon conserved regions within PKS genes were used in Southern hybridizations to identify clones from the *M. echinospora* genomic library that carried putative PKS genes. The Southern hybridizations were performed by methods known in the art. Southern hybridization of the genomic *M. echinospora* cosmid library with a DNA probe designed to target type I PKS genes (KS<sup>I</sup>), (Kakavas, S.J., et al., *J. Bacteriol.*, 179, 7515-7522 (1997)), unveiled five positive clones, which were designated clones 4b, 10a, 13a, 56, and 60. See Figure 1. The same five clones were also identified upon rescreening the genomic library with type II DNA probe (actI). See Figure 1. Although this preliminary analysis clearly demonstrated the presence of *Micromonospora* PKS gene homologues, a secondary screen was performed, as PKS hybridization analyses are often plagued by false hybridization to gene clusters that encode spore pigment biosynthesis.

The second screening was based on the assumption that calicheamicin's biosynthetic cluster would also contain genes encoding for deoxysugar ligand synthesis. Further, it was postulated that all hexopyranosyl ligands of calicheamicin diverged from the common intermediate 4-keto-6-deoxy TDP-D-glucose (30), Figure 5, as macromolecule-sugar synthesis in many organisms began with a similar common intermediate. Thus, it was believed that the cluster encoding for calicheamicin biosynthesis, in addition to carrying a PKS-encoding region, would carry both a common glucose-1-phosphate nucleotidyltransferase and a NDP- $\alpha$ -D-glucose 4,6-dehydratase gene, encoding the putative enzymes E<sub>p1</sub>, and E<sub>od</sub>, respectively. See figure 5. These enzymes are

necessary to convert a sugar (12)(figure 5) to the hypothesized common intermediate, 4-keto-6-deoxy TDP-D-glucose (30). Analogs to 4,6-dehydratases have been previously characterized from *E. coli*, *Salmonella*, and *Streptomyces*. Additionally, a nucleotide transferase from *Salmonella* has been characterized as an alpha-D-glucose-1-phosphate thymidyltransferase. The secondary screen was performed using a probe based upon the postulation that the *M. echinospora*'s calicheamicin synthesis would begin from a similar precursor found in *E. coli*, *Streptomyces* and *Salmonella*, and that this precursor required a dehydratase to convert it into the common intermediate, 4-keto-6-deoxy TDP-D-glucose (30). In particular, a DNA probe (designated E<sub>od</sub><sup>I</sup>) was designed from the conserved NAD<sup>+</sup>-binding site of bacterial NDP- $\alpha$ -D-glucose 4,6-dehydratases. He, X., et al., *Biochem.*, 35, 4721-4731 (1996). Southern hybridization of the genomic *M. echinospora* cosmid library with the E<sub>od</sub><sup>I</sup> probe revealed cross-hybridization with clones 4b, 10a, 13a, 56, and 60. Two additional clones, designated 58 and 66, were also identified in this screen. See Figure 1. This secondary hybridization indicated the clustering of genes encoding both polyketide and deoxysugar biosynthesis.

For final corroboration, since secondary metabolite biosynthesis is typically clustered with resistance genes in actinomycetes, all hybridization-positive clones were tested for their ability to grow in the presence of varying concentrations of calicheamicin. In this final screen, six of the seven hybridizing clones displayed differing levels of resistance to calicheamicin (4b $\approx$ 10a $\approx$ 13a $\geq$ 56 $\geq$ 66 $>$ 60)(See Figure 1) while clone 58 lacked the ability to grow in the presence of calicheamicin. In addition, these resistance screens revealed that clones 4b, 10a, 13a conferred much higher levels of resistance to calicheamicin than the other clones. Upon rescreening the genomic library for

calicheamicin-resistant clones, three additional clones (3a, 4a, and 16a) were found to confer similar levels of resistance. Cumulatively, the results demonstrated that clones 4b, 10a, 13a, 56, and 60 carried PKS I and II homologues and deoxy sugar biosynthetic genes, as well as encoded the gene responsible for conferring calicheamicin-self resistance.

The clones positive for PKS I and II and deoxy sugar biosynthesis homology and calicheamicin resistance were used to map the biosynthetic cluster. Southern hybridization established similarity between clones 3a, 4a, 4b, 10a, 13a, 16a and 56. In addition, nucleotide sequence overlaps were found between clones 4b, 13a, and 56. See Figure 1. Restriction mapping and Southern hybridization of these clones indicated that the positive cosmid clones corresponded to a continuous region of the *M. echinospora* chromosome spanning > 100 kb. The present invention thus provides for cosmids having a nucleic acid molecule from *Micromonospora echinospora* encoding for a nonchromoprotein enediynes biosynthetic cluster.

After isolating the biosynthetic gene cluster and elucidating the sequence, open reading frames ("orfs") were assigned. Tentative gene assignments were derived from amino acid sequence similarity of translated orfs to gene products of known function via direct BLAST (Basic Local Alignment Search Tool) database searches on the amino acid level. Karlin, et al., *Proceed Natl. Acad. Sci., U.S.A.*, 87, 2264-2268 (1990); Karlin, et al., *Proceed Natl. Acad. Sci., U.S.A.*, 90, 5873-5877 (1993); Altchul, *Nature Genet.*, 6, 119-129 (1994). The gene cluster organization is provided in figure 1.

Based on BLAST analysis tentative gene assignments were made. Specifically, there are 15 genes that encode for the aryltetrasaccharide moiety (20,928 bp; *D, E, F, G, H, J, K, N, O, Q, S, T, U, X, W, 6MSAS*), 12 putative genes which encode for the aglycone



(13,284 bp; *P, S, V, W, ActI, ActII, ActIII, OrfI, OrfIII, OrfV, OrfVI, OrfVII*), 13 putative genes involved in membrane transport, regulation, DNA movement and/or resistance (19,704 bp; *A, B, C, I, L, M, R, orf4, orf8, OrfVIII, OrfIX, OrfX, OrfXI, IS-element*), and the remaining 8 genes of unknown function (7383 bp; *orf1, orf2, orf3, orf5, orf6, orf7, OrfII, OrfIV*).

One aspect of the invention relates to transformation of a host cell with *M. echinospora* DNA. This method provides a reproducible transformation efficiency of  $\sim 10^3$  kanamycin resistant transformants/ g DNA using a pKC1139-based vector. The invention further provides that the host cell can be but is not limited to bacteria, yeast, fungus, insect, plant or mammalian. Transformations of bacteria, yeast, fungus, insect, plant or mammalian cells are performed by methods known in the art.

The present invention also provides the isolation and characterization of genes encoding polypeptides involved in calicheamicin resistance such as *orfXI* and *calC*. One aspect of the invention relates to an isolated DNA strand having the gene *calC* and having the DNA sequence SEQ. ID No.: 1. The present invention also relates to an isolated protein CalC, having the amino acid sequence, SEQ ID. NO. 2. The invention further provides for *calC* gene fragments coding for a bioactive CalC polypeptide. The polypeptide, CalC, confers calicheamicin resistance and has 181 amino acids. The invention also provides for CalC fragments conferring calicheamicin resistance.

The *calC* locus was isolated by identifying calicheamicin genomic cosmid clones that were able to grow on luria bertani ("LB") agar plates containing ampicillin and calicheamicin. The DNA of the positive clones (clones that grew on the plates containing calicheamicin) was isolated and subsequent restriction mapping localized the desired

phenotype (calicheamicin resistance). The DNA was then sequenced and the open reading frames analyzed to ascertain the orf encoding for the desired phenotype. *In vitro* studies were also performed and confirmed the ability of CalC to inhibit DNA cleavage.

DNA containing *calC* was cloned into an inducible vector, using known methods, resulting in overexpression of *calC*. The polypeptide product (CalC) was then isolated and purified to homogeneity. Analysis of the purified CalC revealed that it is a non-heme iron metalloprotein that functions via inhibition of calicheamicin-induced DNA cleavage *in vitro*. Another aspect of the invention is an expression vector containing *calC* or a fragment of *calC* encoding for a bioactive molecule. There is also provided a transformed host cell, preferably bacteria, more preferably *E. coli*, containing *calC* or a fragment of *calC* encoding for a bioactive molecule. Such transgenic expression of *calC* results in an  $10^5$ -fold increase in calicheamicin resistance in *E. coli*, a 100-fold increase in resistance in *S. lividans*, and a 50-fold increase in resistance in yeast.

The present invention provides for the transformation of human cells with the *calC* gene. The transgenic expression of *calC* in the HT1080 (human) cell line increased its resistance to calicheamicin 10-fold. This technique allows bone marrow cells, for example, to be removed from a patient being treated with calicheamicin, and for these cells to be transformed with *calC*, and for the transformed cells to be returned to the patient. This allows the patient to tolerate treatment with calicheamicin or allows the patient to receive higher doses of calicheamicin as the returned human-*calC*-transformed cells have calicheamicin resistance. The transformation is performed by methods known in the art. The embodiment of the invention would be applicable to many diseases being treated with calicheamicin.

The invention further provides for a method of assaying the calicheamicin-induced DNA cleavage and its CalC-mediated inhibition using the molecular break light assay. Two molecular break lights (MLBs) for the experiments are described in example 7. Break light A is comprised of a 10-base pair stem which contained the known calicheamicin recognition sequence 5'-TCCT-3', while break light B carries the *Bam*HI endonuclease recognition sequence 5'-GGATCC-3'. The 5'-fluorophore of both probes was fluorescein (FAM, absorbance<sub>max</sub> = 485 nm, emission<sub>max</sub> = 517 nm) while the corresponding 3'-quencher was 4-(4'-dimethylaminophenylazo)benzoic acid (DABCYL). Generally, MLBs operate by a separation of the fluorophore-quencher pair resulting a corresponding fluorescent signal. The molecular break lights, as illustrated in figure 13, operate through cleavage of the stem by specific enzymatic or non-enzymatic nuclease activity resulting in the separation of the fluorophore-quencher pair and corresponding fluorescent signal (see figure 14). CalC in a two-fold molar excess of calicheamicin, completely abolishes calicheamicin mediated DNA cleavage as monitored by the break light assay (see figure 15).

CalC acts as a "cleavage sink". In essence the protein is cleaved as an alternative to the desired DNA target. Thus, the invention provides the first such demonstrated mechanism for resistance to a cleavage agent and explains why CalC is able to function in all organisms tested so far (i.e. *E.coli*, *S.lividans*, yeast, and humans).

The invention further provides for the use of the break light assay to determine calicheamicin titers during production of thereof. Furthermore, the molecular break light assay may be used to determine the DNA cleavage activity of calicheamicin analogs generated using the techniques of this invention.

Another aspect of the invention relates to an isolated DNA strand containing the *calH* gene having the DNA sequence SEQ ID. No: 3. The invention also relates to the polypeptide CalH, having amino acid sequence SEQ ID. No. 4. The invention further provides for *calH* gene fragments coding for a bioactive CalH. CalH is involved in the formation of the aryltetrasaccharide 4,6-dideoxy-4-hydroxylamino-D-glucose moiety. CalH catalyzes the conversion of intermediate (30) to intermediate (39) (figure 5). CalH is a TDP-6-deoxy-D-glycerol-L-threo-4-hexulose 4-transaminase, which catalyzes a pyridoxal phosphate ("PLP")-dependent transamination from glutamate to provide 4-amino-6-deoxy TDP-D glucose (intermediate 39)(figure 5). The invention also provides for CalH fragments that retain bioactivity. There is also provided an expression vector containing the *calH* gene or fragments of the *calH* gene that encode for a bioactive polypeptide. CalH were overexpressed as a (histidine)<sub>10</sub>-fusion protein and subsequently purified by nickel affinity chromatography.

According to BLAST analysis, CalH closely resembles perosamine synthase, an enzyme which converts compound 30 to compound 39 (See figure 5) *en route* to the biosynthesis of TDP-perosamine (TDP-4,6-dideoxy-4-amino-D-mannose) in *E. coli*. Wang, L., et al., *Infect. Immunol.*, 66, 3545-3551 (1998). Thus CalH is believed to be a 4-ketohexose aminotransferase. To confirm the tentative BLAST assigned function, a combinatorial biosynthesis was performed. Specifically the *calH* gene from calicheamicin was incorporated into a mutant strain of *Streptomyces venezuela*. The 4-dehydrase gene (*des1*) in the methymycin/pikromycin pathway was deleted in this mutant strain. A promoter sequence from the *S. venezuela* methymycin/pikromycin cluster was incorporated in the expression vector to drive the expression of foreign genes (the *calH* of

calicheamicin) in *S. venezuela*. In wild type *S. venezuela* methymycin/pikromycin pathway is known to produce methymycin, neomethymycin, pikromycin, and narbomycin. See figure 6. Deletion of the *des1* gene in the mutant strain led to the accumulation of the CalH substrate, TDP-4-keto-6-deoxyglucose (compound 30, figure 6). The constructed expression vector with the *S. venezuela* promoter expressed the *calH* gene to make the CalH protein. CalH acted on the substrate, 30, to produce compound 39 (figure 6). Compound 39 in turn, with the action of *S. venezuela*'s DesVII (a glycosyltransferase) produced two methymycin/pikromycin-calicheamicin hybrid compounds. See Figure 6, compounds 40 and 41. These hybrid compounds carry the 4-aminohexose ligand of calicheamicin. This work provides indisputable support for the *calH* gene assignment as encoding the TDP-6-deoxy -D-glycero-L-threo-4-hexulose 4-aminotransferase of the calicheamicin pathway. The CalH acted on the TDP-4-keto-deoxyglucose substrate (compound 30) to produce compound 39. (Figure 5).

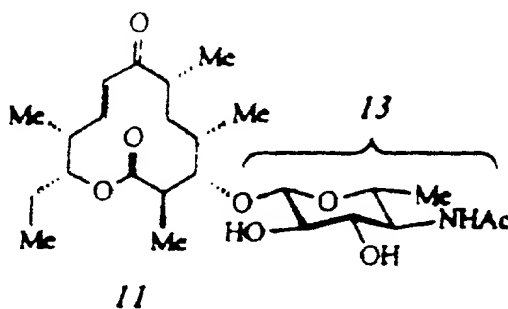
Moreover, CalH is able to directly mediate the synthesis of the product TDP-4,6-dideoxy-alpha-D-glucose as demonstrated by HPLC isolation of the product and confirmation by high-resolution mass spectrometry. In addition this compound was found to co-elute with chemically synthesized TDP-4-amino-4,6-dideoxy-alpha-D-glucose.

In addition, these results reinforce the indiscriminate nature of the corresponding glycosyltransferase (DesVII) as they reveal that the glycosyltransferase (DesVII) of the *S. venezuela* pathway can recognize alternative sugar substrates whose structures are considerably different from the original amino sugar substrate, TDP-D-desosamine. The results also clearly demonstrate the ability to engineer secondary metabolite glycosylation through a rational selection of gene combinations. The successful expression of the CalH

protein in *S. venezuela* by the newly constructed expression vector highlights the potential of using this system to express other foreign genes in this strain.

Thus, one aspect of the present invention further relates to the construction of a composite gene cluster having the ability to make and attach non-natural sugars. The invention further provides an expression vector having a calicheamicin gene operably linked to regulatory sequences to control expression of the calicheamicin protein, and preferably the regulatory sequence is a *Streptomyces* promoter. The present invention also relates to two newly synthesized sugars, compound (11) and compound (12)(figure 7).

Compound 11 has the formula:

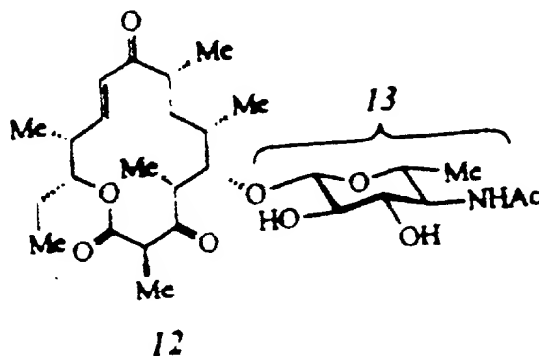


The spectral data of compound 11 was as follows:

$^1\text{H}$  NMR (500 MHz  $\text{CDCl}_3$ , J in hertz)  $\delta$  6.75 (III, dd, J = 16.0, 5.5, 9-H) 6.44 (1H, dd, J = 16.0, 1.2, 8-H), 5.34 (1H, d, j = 8.0, N-H), 4.96 (1H, m, 11-H), 4.27 (1H, d, J=7.5, 1-H), 3.66 (1H, dd, J = 9.5, 8.0, 4'-H), 3.60 (1H, d, J = 10.5, 3-H), 3.50 (1H, 1, J - 9.5, 3'H), 3.<sup>d</sup> (1H, m, 5'-H), 3.4 (1H, m, 2'-H), 2.84 (1H, dq, J = 10.5, 7.5, 2-H), 2.64 (1H, m, 10-H), 2.53 (1H, m, 6-H), 2.06 (3H, s, Me-C=O), 1.7 (1H, m, 12-H), 1.66 (1H, m, 5-H), 1.56 (1H, m, 12-H), 1.4 (1H, M, 5-H), 1.36 (3H, d., J=7.5, 2-Me), 1.25 (3H, d, J = 6.5, 5'-

Me), 1.24 (1H, m, 4-H), 1.21 (3H, d,  $J=7.5$ , 6 Me), 1.10 (3H, d,  $J=6.5$ , 10-Me), 0.99 (3H, d,  $J=6.0$ , 4-Me), 0.91 (3H, t,  $J=7.2$ , 12-Me);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  205.3 (C-7), 175.1 (C-1), 171.9 (Me-C-O), 147.1 (C-9), 126.1 (C-8), 103.0 (C-1'), 85.8 (C-3), 75.8 (C-5'), 75.8 (C-3'), 74.1 (C-11) 70.8 (C-2'), 57.6 (C-4'), 45.3 (C-6), 44.0 (C-2), 38.1 (C-10), 34.2 (C-5), 33.6 (C-4), 25.4 (C-12), 23.7 (Me-C-O), 18.1 (C-6'), 17.9 (6 Me), 17.6 (4-Me), 16.4 (2-Me), 10.5 (12-Me), 9.8 (10-Me). High-resolution FAB-MS calculated for  $\text{C}_{25}\text{H}_{42}\text{NO}_8$  ( $\text{M} + \text{H}^+$ ) 484.2910, found 484.2303.

Compound 12 has the formula:



The spectral data of compound 12 was as follows:

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ,  $J$  in hertz)  $\delta$  6.69 (1H, dd,  $J = 16.0, 6.0$ , 11-H), 6.09 (1H, dd,  $J = 16.0, 1.5$ , 10-H), 5.35 (1H, d,  $J = 8.5$ , N-H), 4.96 (1H, m, 13-H), 4.36 (1H, d,  $J = 7.5$ , 1'-H), 4.19 (1H, m, 5-H), 3.83 (1H-q,  $J=6.5$ , 2-H), 3.68 (1H, dt,  $J=10.0, 8.5$ , 4'-H), 3.52 (1H, t,  $J = 8.5$ , 3'-H), 3.50 (1H, m, 5-H), 3.42 (1H, t,  $J = 7.5$ , 2'-H), 2.92 (1H, dq,  $J = 7.0, 5.0$ , 4-H), 2.81 (1H, m, 8-H), 2.73 (1H, t,  $J=7.5$ , 2'-H), 2.06 (3H, s, Me-C-O), 1.8 (1H, m, 6-H), 1.6 (1H, m, 14-H), 1.55 (1H, m, 7-H), 1.37 (3H, d,  $J = 6.5$ , 2-Me), 1.32 (3H, d,

J = 7.0, 4-Me), 1.3 (1H, m, H-14), 1.27 (3H, d, J = 6.5, 5'-Me), 1.25 (1H, m, 7-H), 1.12 (3H, d, J=6.0, 8-Me), 1.11 (3H, d, J = 6.5, 12-Me), 1.07 (3H, d, J = 6.0, 6-Me), 0.91 (3H, 1, J -7.2, 1 + Me); high resolution FAB MS calculated for C<sub>28</sub> H<sub>46</sub> NO<sub>2</sub> (M+H<sup>+</sup>) 540.3172, found 540.3203.

One aspect of the invention relates to an isolated DNA strand containing the *calG* gene and having the DNA sequence SEQ ID. NO.: 5. Another aspect of the invention is the protein, CalG, having amino acid sequence SEQ ID. No.: 6. According to BLAST analysis, *calG* encodes a 4,6-dehydratase. Dehydratases had been characterized from *E. coli*, *Salmonella* and *Streptomyces*, (Thompson, M. et al., *J. Gen. Microbiol.*, 138, 779-786 (1992); Vara, J.A., et al., *J. Biol. Chem.*, 263, 14992-14995 (1988)), and analogous NDP-D-glucose 4,6-dehydratases had been characterized from a variety of organisms. Liu, H.-w., et al., *Ann. Rev. Microbiol.*, 48, 223-256 (1994); Hallis, T.M., et al., *Acc. Chem. Res.*, in press (1999). Based upon these prior studies, it was known that the overall transformation catalyzed by 4,6-dehydratases is an intramolecular oxidation-reduction where an enzyme-bound NAD<sup>+</sup> receives the 4-H as a hydride in the oxidative half-reaction and passes the reducing equivalents to C-6 of the dehydration product in the reductive half-reaction. Thus, it appears that Cal G is necessary for the formation of the aryltetrasaccharide 4,6-dideoxy-4-hydroxylamino-D-glucose moiety. CalG appears to be a TDP-D-glucose 4,6-dehydratase which catalyzes the conversion of intermediate 13 into intermediate 30. (See figure 5). Another aspect of the invention is an expression vector containing *calG* or a fragment of *calG* encoding for a bioactive molecule. There is also provided a transformed host cell, preferably bacteria, more preferably, *E. coli*, containing *calG* or a fragment of *calG* encoding for a bioactive molecule.



Moreover, CalG is able to directly mediate the synthesis of the product TDP-4-keto-6-deoxy-alpha-D-glucose as demonstrated by an assay where in the product is known to absorb at 320 nm under basic conditions. In addition this compound was found to co-elute with chemically synthesized TDP-4-keto-6-dideoxy-alpha-D-glucose. CalG has been demonstrated to utilize UDP-glucose as a substrate.

There is also disclosed an isolated DNA strand containing the *calS* gene. Based on sequence homology with other P450-oxidases, CalS appears to be a P450-oxidase homolog which performs the oxidation of intermediate 39 to intermediate 42 (figure 5). The oxidation may occur at the nucleotide sugar level or hydroxylamine formation after the sugar has been transferred to the aglycone. There is also provided an expression vector containing the *calS* gene or a fragment of *calS* encoding for a bioactive molecule. There is also provided a transformed host cell, preferably bacteria, more preferably *E. coli*, containing *calG* or a fragment of *calG* encoding for a bioactive molecule.

There is also disclosed an isolated DNA strand containing the *calQ* gene. Based on sequence homology, CalQ appears to be a UDP-D-glucose-6 dehydrogenase homolog. The CalQ assay is based upon the requirement of this enzyme for two equivalents of NAD<sup>+</sup> for activity. Thus, an assay based upon the increase in absorbance (as a result of the conversion of NAD<sup>+</sup> to NADH upon the conversion of UDP-alpha-D-glucose to UDP-alpha-D-glucuronic acid). The product was also shown to co-elute with commercially available UDP-glucuronic acid and separately confirmed by high resolution mass spectrometry. This enzyme was also shown to utilize TDP-glucose.

There is also provided an expression vector containing the *calQ* gene or a fragment of *calQ* encoding for a bioactive molecule. There is also provided a transformed host cell,

preferably bacteria, more preferably *E. coli*, containing *calQ* or a fragment of *calQ* encoding for a bioactive molecule.

The present invention allows genetic manipulation of the biosynthetic gene cluster to produce calicheamicin analogs. The present invention provides for producing calicheamicin analogs by constructing deletions or substitutions of the genes involved in biosynthesis of the aryltetrasaccharide. The invention further provides for *in vitro* glycosylation by altering the glycosylation pattern of calicheamicin (via a glycosyltransferase) to produce additional analogs. The invention also provides for alteration of the calicheamicin aglycone by genetic manipulation of the genes encoding the biosynthesis of the warhead. Genetic manipulation, such as producing deletions or substitutions are performed using methods known in the art.

The invention provides for a method of purifying calicheamicin through affinity chromatography. Because of its homology with calicheamicin, CalC functions as a calicheamicin-sequestering/binding protein. Affinity chromatography is performed using methods known in the art.

The invention relates to the expression of the genes located in the biosynthetic gene cluster by using methods known in the art to insert the genes into a suitable expression vector and operably linking the gene to regulatory sequences to control expression of the gene to produce the protein encoded by the inserted gene. The present invention also provides for expression of biologically active proteins by inserting fragments of genes selected from the biosynthetic gene cluster, which encode for biologically active proteins, into a suitable expression vector, using methods known in the art. The genes would be operably linked to regulatory sequences to control their expression.

The term "hybridization" as used herein is generally used to mean hybridization of nucleic acids at appropriate conditions of stringency as would be readily evident to those skilled in the art depending upon the nature of the probe sequence and target sequences. Conditions of hybridization and washing are well known in the art, and the adjustment of conditions depending upon the desired stringency by varying incubation time, temperature and/or ionic strength of the solution are readily accomplished. See, for example, Sambrook, J. et al., *Molecular Cloning: A Laboratory Manual*, 2nd edition, Cold Spring Harbor Press, Cold Spring Harbor, New York, 1989. The choice of conditions is dictated by the length of the sequences being hybridized, in particular, the length of the probe sequence, the relative G-C content of the nucleic acids and the amount of mismatches to be permitted. Low stringency conditions are preferred when partial hybridization between strands that have lesser degrees of complementarity is desired. When perfect or near perfect complementarity is desired, high stringency conditions are preferred. For typical high stringency conditions, the hybridization solution contains 6x S.S.C., 0.01 M EDTA, 1x Denhardt's solution and 0.5% SDS. Hybridization is carried out at about 68°C for about 3 to 4 hours for fragments of cloned DNA and for about 12 to about 16 hours for total eukaryotic DNA. For lower stringencies the temperature of hybridization is reduced to about 12°C below the melting temperature (T<sub>M</sub>) of the duplex. The T<sub>M</sub> is known to be a function of the G-C content and duplex length as well as the ionic strength of the solution.

As used herein, the term "substantial sequence identity" or "substantial homology" is used to indicate that a nucleotide sequence or an amino acid sequence exhibits substantial structural or functional equivalence with another nucleotide or amino acid sequence. Any structural or functional differences between sequences having substantial

sequence identity or substantial homology will be *de minimis*; that is, they will not substantially affect the ability of the sequence to function as indicated in the desired application. Differences may be due to inherent variations in codon usage among different species, for example. Structural differences are considered *de minimis* if there is a significant amount of sequence overlap or similarity between two or more different sequences or if the different sequences exhibit similar physical characteristics even if the sequences differ in length or structure. Such characteristics include for example, ability to hybridize under defined conditions, or in the case of proteins, immunological crossreactivity, similar enzymatic activity, etc.

Additionally, two nucleotide sequences are "substantially complementary" if the sequences have at least about 40 percent, more preferably, at least about 60 percent and most preferably about 90 percent sequence similarity between them. Two amino acid sequences are "substantially homologous" if they have at least 40%, preferably 70% similarity between the active portions of the polypeptides.

As used herein, the phrase "hybridizes to a corresponding portion" of a DNA or RNA molecule means that the molecule that hybridizes, e.g., oligonucleotide, polynucleotide, or any nucleotide sequence (in sense or antisense orientation) recognizes and hybridizes to a sequence in another nucleic acid molecule that is of approximately the same size and has enough sequence similarity thereto to effect hybridization under appropriate conditions. It is to be understood that the size of the "corresponding portion" will allow for some mismatches in hybridization such that the "corresponding portion" may be smaller or larger than the molecule which hybridizes to it, for example 20-30% larger or smaller, preferably no more than about 12-15 % larger or smaller.

The term "functional derivative" of a nucleotide sequence (or poly- or oligonucleotide) is used herein to mean a fragment, variant, homolog, or analog of the nucleotide sequence of interest or of the nucleotide sequence encoding the peptide of interest. A functional derivative may include alternative codons for amino acids, or may code for different amino acids which do not substantially change the function of interest of the peptide encoded by the nucleotide. A functional derivative may retain at least a portion of the function of the nucleotide sequence of interest or of the nucleotide sequence encoding the peptide of interest, which function permits its utility in accordance with the invention. Such function may include the ability to hybridize with at least one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, or 94; the ability to hybridize with a substantially homologous DNA from another organism which DNA encodes at least one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 and 95 or a functional derivative thereof, or with an mRNA transcript thereof, or the ability to encode a protein that is a functional derivative of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 and 95, or the like.

A "fragment" of the gene or nucleotide sequence refers to any subset of the molecule, e.g., a shorter polynucleotide or oligonucleotide. A "variant" refers to a molecule substantially similar to either the entire gene or a fragment thereof, such as a nucleotide substitution variant having one or more substituted nucleotides, but which

maintains the ability to hybridize with the particular gene or to encode mRNA transcript which hybridizes with the native DNA. A "homolog" refers to a fragment or variant sequence from a different genus or species. An "analog" refers to a non-natural molecule substantially similar to or functioning in relation to either the entire molecule, a variant or a fragment thereof.

"Functional derivatives" of the proteins as described herein are fragments, variants, analogs, or chemical derivatives of at least one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 and 95, and which retain at least a portion of the activity of at least one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 and 95 or retain immunological cross reactivity with an antibody specific for at least one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 and 95. As used herein, a fragment of the protein refers to any subset of the molecule. Variant peptides may be made by direct chemical synthesis, for example, using methods well known in the art. An analog of a protein refers to a non-natural protein substantially similar to either the entire protein or a fragment thereof. As used herein, a chemical derivative of a protein may contain additional chemical moieties not normally a part of the peptide or peptide fragment. Modifications may be introduced into the a peptide or fragment thereof by reacting targeted amino acid residues of the peptide with an organic derivatizing agent that is capable of reacting with selected side chains or terminal residues.

A protein or peptide according to the invention may be produced by culturing a cell transformed with a nucleotide sequence of this invention (in the sense orientation), allowing the cell to synthesize the protein and then isolating the protein, either as a free protein or as a fusion protein, depending on the cloning protocol used, from either the culture medium or from cell extracts. Alternatively, the protein can be produced in a cell-free system. Ranu, et al., *Meth. Enzymol.*, 60:459-484, (1979).

As can be appreciated from the disclosure above, the present invention has a wide variety of applications. Accordingly, the following examples are offered by way of illustration, not by way of limitation.

## EXAMPLES

### Example 1

To rapidly elucidate the nucleotide sequence, thermocycle sequencing was accomplished from pUC- or pBluescript-based subclones (using M13 primers and primer walking) as well as directly from isolated cosmids (via primer walking). Nucleotide sequence data was acquired using two Applied Biosystems automated 310 genetic analyzers and sequences were subsequently assembled using the Applied Biosystems AutoAssembler™ DNA sequence assembly software. Dear, S., et al., *Nucl Acids Res.*, 14, 3907-3911 (1991); Huang, X., *Genomics*, 14, 18-25 (1992). Orf assignments were accomplished using a combination of the computational programs MacVector™ 6.0 and Brujene. MacVector is a commercially available software package which provides the ability to construct a *Micromonospora* codon bias table (from known *Micromonospora* sequences) and subsequently use this codon bias table to search for optimal orfs. Fickett,

J.W., *Nucleic Acids Research*, 10, 5303-5318 (1982). Alternatively, the shareware program Brujene was specifically designed for streptomycetes and assigns priority to orfs that illustrate a consistency high G/C% in the wobble position.

### Example 2: Isolating and Characterizing *calC*

To isolate the gene(s) responsible for calicheamicin resistance in *Micromonospora*, clones conferring calicheamicin resistance were selected by growth of a *Micromonospora* genomic bifunctional cosmid library on LB plates containing ampicillin (50  $\mu\text{g ml}^{-1}$ ) and calicheamicin (0.25  $\mu\text{g ml}^{-1}$ ). In this selection, six clones (3a, 4a, 4b, 10a, 13a and 16a) displayed resistance to calicheamicin. Restriction mapping of these clones localized the desired phenotype to a ~2kb *Pst*I-*Sac*I fragment of DNA. (Figure 2). Maximum tolerated concentrations of calicheamicin on the LB plates was ascertained. The results are as follows:

Cosmid or Plasmid	Maximum tolerated concentration of calicheamicin
cosmids 3a, 4a, 10a, 13a, and 16a	0.5 $\mu\text{g ml}^{-1}$
pJT1214 and pJT1232	5.0 $\mu\text{g ml}^{-1}$
pRE7	20.0 $\mu\text{g ml}^{-1}$
induced pRE7	50.0 $\mu\text{g ml}^{-1}$
pJT1224 , pAP6, Pre1, and control plasmids pUC18, pBluescript, and pMAL-	<0.01 $\mu\text{g ml}^{-1}$



C2	
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Nucleotide sequence analysis of the *PstI-SacI* fragment suggested that it contained two possible orfs. The proximal 1 kb of this fragment carried the single orf *calD* while the distal 1 kb presented orf *calC*. Computer translation of *calC* and subsequent BLAST analysis revealed no homology with known proteins, while the translation of *calD* to its respective protein, CalD, revealed the presence of three amino acid motifs typically conserved in S-adenosylmethionine-utilizing O-methyltransferases. Therefore, it was hypothesized that *calD* was not responsible for calicheamicin resistance. To rule out *calD* as being responsible for calicheamicin resistance, a subclone was engineered (*pJT1224*) to contain an intact *calD*, but the truncated *calC* gene. This subclone was not able to confer resistance to calicheamicin. Next, a subclone containing the *calC* region was constructed (*pJT1232*). This clone conferred calicheamicin resistance, as indicated in the above chart.

To ascertain the amino acid sequence of CalC and learn its properties, *calC* was cloned into a pMAL-C2 vector. (pMAL-C2 by itself could not confer calicheamicin resistance. See above chart.) The resulting plasmid, pRE7, which contained *calC*, conferred resistance to calicheamicin. See above chart. Plasmid pRE7 was then induced with isopropyl Beta-D-thiogalactoside ("IPTG") to overexpress CalC. Induced pRE7 conferred resistance to calicheamicin and produced a maltose-binding protein CalC fusion protein (mbp-CalC). This resulting overexpression of CalC increased calicheamicin resistance  $10^2$ -fold *in vivo*. See above chart.

### Example 3: Expression of protein CalC

The protein mbp-CalC was overexpressed and purified for further analysis. The mbp-CalC was purified from pRE7/*E. coli* to homogeneity as judged by SDS-PAGE. An overnight LB culture (containing 50 mg ml<sup>-1</sup> ampicillin and 50 ng ml<sup>-1</sup> calicheamicin from a fresh pRE7/*E. coli* colony was grown at 37 °C, 250 rpm to an A<sub>600</sub>=0.5, induced with 0.5 mM IPTG and growth continued overnight. Cells were harvested (4,000 x g, 4 °C, 20 minutes), resuspended in buffer A (50mM Tris-Cl, pH 7.5, 200 mM NaCl, 1mM EDTA) and disrupted by sonication. The cell debris was removed by centrifugation (5,000xg, 4°C, 20 minutes). The supernatant was applied to an amylose affinity column (1.5 x 7.0 cm, 1 mL min<sup>-1</sup>). The desired mbp-CalC protein was eluted with buffer A containing 10 mM maltose. The eluate was concentrated and chromatographed on an S-300 column (50mM Tris-Cl, pH 7.5, 200 mM NaCl). Active fractions were used immediately or frozen at -80°C for storage.

### Example 4: Verification of CalC's calicheamicin resistance

Given that calicheamicin leads to double strand DNA cleavage and CalC provides calicheamicin-resistance *in vivo*, it was expected that the addition of CalC to an *in vitro* calicheamicin-induced DNA cleavage assay would inhibit DNA cleavage. To test this theory, preliminary assays were performed with supercoiled pBluescript plasmid DNA ("pBS") as the template, and dithiothreitol ("DTT") as the reductive initiator. In a typical assay, purified mbp-CalC (15.0 nM) and 30.0 nM calicheamicin were preincubated for 15 min. in a total volume of 25 µL 40 mM Tris-Cl, pH 7.5, at 37 °C. Then 2.5 µL 10mM DTT stock solution was added to the assay solution, and the assay was incubated an

additional 1 hour at 37°C. DNA fragmentation was assessed by electrophoresis on a 1% agarose gel stained with ethidium bromide. Using this assay, it was found that mbp-CalC could completely inhibit calicheamicin-induced DNA cleavage at concentrations nearing 10<sup>3</sup>-fold excess of calicheamicin. Preincubation of mbp-CalC and DTT, protein removal via forced dialysis, and the subsequent use of the DTT solution as reductant did not noticeably affect the amount of DNA cleavage.

As indicated in Figure 4(b), no DNA cleavage was observed in the absence of DTT or calicheamicin (lanes a and b), while efficient cleavage was demonstrated in the presence of DTT and calicheamicin (lane c). As expected, the addition of mbp-CalC completely inhibited calicheamicin-induced DNA cleavage (lane f) while the addition of mbp alone (lane d) as a control, failed to inhibit calicheamicin-induced DNA cleavage. Furthermore, preincubation of mbp-CalC with DTT (not shown), or *apo*-mbp-CalC (lacking the Fe cofactor)(lane e), also failed to inhibit calicheamicin-induced DNA cleavage. However, the addition of Fe<sup>+2</sup> or Fe<sup>+3</sup> to the *apo*-mbp-CalC assay could reconstitute CalC activity (lane g). Reconstitution of *apo*-mbp-CalC was accomplished by preincubation with 1 mM FeSO<sub>4</sub> (Fe<sup>+2</sup>) or FeCl<sub>3</sub> (Fe<sup>+3</sup>) prior to the activity assay as previously described.

### **Example 5: Production of methymycin/pikromycin-calicheamicin hybrid compounds**

The 1.2 kb *calH* gene was amplified by polymerase chain reaction (PCR) from pJST1192<sub>kpn7</sub>, which is a subclone containing a 7.0 kb *KpnI* fragment of cosmid 13a. The amplified gene was cloned into the *EcoRI/XbaI* site of the expression vector pDHS617. This expression vector contains an apramycin resistance marker. The plasmid pDHS617 was derived from pOJ1446 (Bierman, M. et al., *Gene* 1992, 116, 43-49). A promoter

sequence from the *S. venezuela* methymycin/pikromycin cluster was incorporated in the plasmid to drive the expression of foreign genes in *S. venezuela*. The resulting plasmid, pLZ-C242 (containing the *calH* gene insert and the promoter sequence) was introduced by conjugal transfer using *E.coli* S 17-1 into a previously constructed *S. venezuela* mutant, *desI*. (Borisova, S. et al., *Org. Lett.* 1999. 1. 133-136). In the *DesI* mutant, the *desI* was replaced by the neomycin resistance gene, which confers resistance to kanamycin. The pLZ-C242-containing *S. venezuela-DesI* colonies were identified on the basis of their resistance to apramycin antibiotic. One of these positive colonies, *DesI/calH-1* was grown in 100 ml of seed medium at 29°C for 48 hours and then inoculated and grown in five Liters of vegetative medium. Cane, D.E., et al., *J. Am. Chem. Soc.*, 1993, 115, 522-526. The culture was centrifuged to remove cellular debris and mycelia. The supernatant was adjusted to pH 9.5 with concentrated KOH, followed by chloroform extraction. The crude products (700 mg) were subjected to flash chromatography on silica gel using a gradient of 1-20% methanol in chloroform. A major product, 10-deoxymethynolide (ca. 400 mg), and a mixture of two minor macrolide compounds were obtained. The two macrolides were further purified by HPLC on a C<sub>18</sub> column using an isocratic mobile phase of acetonitrile/H<sub>2</sub>O (1:1). They were later identified as compound (11) and compound (12)(figure 7) by spectral analyses.

#### **Example 6: Molecular Break Light Assay**

The invention further provides for a method of assaying the calicheamicin-induced DNA cleavage and its CalC mediated inhibition using the molecular break light assay. Two molecular break lights for the experiments are shown in Fig. 13. Break light A was

comprised of a 10-base pair stem which contained the known calicheamicin recognition sequence 5'-TCCT-3', while break light B carried the *Bam*HI endonuclease recognition sequence 5'-GGATCC-3'. The length of break light B also considered the requirement of a 3 base pair overhang required for *Bam*HI recognition and the stem of break light A was adjusted to a comparable length and melting temperature. The loop of both probes consisted of a T<sub>4</sub> loop to ensure non-hybridizing interactions. The 5'-fluorophore of both probes was fluorescein (FAM, absorbance<sub>max</sub> = 485 nm, emission<sub>max</sub> = 517 nm) while the corresponding 3'-quencher was 4-(4'-dimethylaminophenylazo)benzoic acid (DABCYL). Previous studies have shown DABCYL to serve as a universal quencher in molecular beacons and there is significant spectral overlap ( $1.02 \times 10^{-15} \text{ M}^{-1} \text{ cm}^3$ ) between the emission spectrum of FAM and the absorption spectrum of DABCYL. In a typical molecular beacon, the quenching efficiency of this pair via FRET has been shown to be essentially complete (99.9%), providing a significant enhancement of the signal to noise ratio as compared to typical complementary oligonucleotide pair FRET-based assays.

*Enzymatic Cleavage as Proof of Principle.* The first test was to demonstrate the specificity of the designed molecular break lights via enzymatic cleavage. Specifically, only break light B should cleave in the presence of the restriction endonuclease *Bam*HI while both A and B should be digested by the non-specific nuclease DNaseI. As anticipated, Fig. 14a reveals a time dependent and [*Bam*HI]-dependent increase of fluorescence only with B while A shows no change at 37 °C. Fig. 14b illustrates an increase of fluorescence over time with either break light A or B when digested with DNaseI which is also [DNaseI]-dependent. In comparison, control samples containing break lights alone or break lights in the presence of BSA gave no change in fluorescence

over > 2 hr at 37 °C. Given the lack of fluorescence in the absence of enzyme, the designed break lights show no appreciable melting at the designated assay temperature. Furthermore, these experiments clearly demonstrate the specificity of cleavage by *Bam*HI for B and, for the first time, illustrate the principle application of molecular break lights to assess DNA cleavage.

Interestingly, the fluorescence maximum intensity obtained upon complete *Bam*HI cleavage was only 75% that observed in the presence of DNaseI at the same concentration of molecular break light. Furthermore, after the *Bam*HI reaction was complete, the addition of *Bam*HI showed no change while the addition of DNaseI resulted in additional cleavage to give the expected 100% fluorescence maximum. This observation suggests the poly-guanidine tail left attached to FAM upon *Bam*HI digestion quenches the fluorescent signal by ~25%. Consistent with this finding, PAGE analysis of the reaction products confirmed the presence of a 3-base overhang after excess treatment with *Bam*HI which is completely degraded upon DNaseI digestion. As a result, the fluorescence maximum observed with excess *Bam*HI was designated 100% cleavage for the *Bam*HI kinetic studies described below.

*Enediyne-Catalyzed Cleavage.* Previous assays for enediyne cleavage of DNA relied upon discontinuous assays using radioactive DNA probes, electrophoresis and subsequent phosphorimager analysis. In contrast, by using break lights one can directly follow the extent of DNA cleavage by a specific enediyne in real time with high sensitivity. To demonstrate, Fig. 15a,b and Fig. 16a,c,d illustrate cleavage of break light A with varying concentrations of either (1) naturally-occurring enediynes including esperamicin, (2), non-enediyne small molecule agents (such as bleomycin (3) methidiumpropyl-Fe-EDTA, (4),

and Fe-EDTA, (5)) as well as the restriction endonuclease *Bam*HI) in the presence of excess reductive activator DTT. Under the conditions described, this assay allows the detection of **1** in the pM range. This sensitivity compares to that of the biochemical induction assay (BIA), the method of choice in detecting DNA-damaging agents. Furthermore, the sensitivity can be significantly enhanced by simply increasing the concentration of the molecular break light in the assay as demonstrated with the iron-dependent agents. The observed maximum fluorescence obtained upon cleavage of 3.2 nM break light A with either **1** or **2** was identical to that observed with DNaseI, consistent with complete degradation of the oligonucleotide. As controls, incubation of molecular break light A with either DTT or enediyne alone revealed no change in fluorescence. Furthermore, although there is some debate regarding the “specificity” of **1**, molecular break light B was cleaved by **1** at an identical rate. This supports the view that the specificity of **1** is more dependent upon context and perhaps less so on DNA sequence. It should also be noted that **1** leads to predominately double-stranded cleavage while **2** provides single-stranded nicks and the current molecular break light assay can not distinguish these two phenomena.

Interestingly, two distinct rates were observed in the enediyne molecular break light assay. The first (0-50 seconds) is a lag time most likely attributed to the enediyne activation while the second (50-200 seconds) is indicative to the initial velocity of DNA cleavage. To confirm this, assays were also established in which DTT and enediyne were first preincubated for 1-5 min followed by initiation via the addition of the substrate oligonucleotide. In these preincubation experiments, the previously observed “lag time” attributed to activation was no longer evident while the initial velocity of DNA cleavage

was identical to that determined in the standard assay. Preincubation for longer periods (> 30 min) revealed the same phenomenon, suggesting “activated” enediynes are perhaps more stable in an aqueous aerobic environment than previously estimated.

*CalC inhibits calicheamicin mediated DNA cleavage.* As illustrated in figure 17, CalC directly inhibits of calicheamicin-mediated DNA cleavage in the break light assay. 3.6pM break light A is coincubated with 3.5nM calicheamicin with increasing amounts of CalC (0.0nm, 1.3nm, 2.6nm, 3.9nm, 5.2nm). Complete inhibition of calicheamicin is achieved with roughly 2-fold excess of CalC. CalC has no effect on esperamicin-induced cleavage of DNA (data not shown).

All publications, patents and patent applications referred to herein are incorporated in this application by reference in their entirety to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety.



## CLAIMS

1. An isolated nucleic acid molecule from a nonchromoprotein enediyne biosynthetic gene cluster from *Micromonospora echinospora* comprising said nucleic acid molecule, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a protein or proteins, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a biologically active fragment of a protein or proteins, a single-stranded nucleic acid molecule derived from said nucleic acid molecule, or a single-stranded nucleic acid molecule derived from a portion or portions of said nucleic acid molecule.
2. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule comprises at least one of *calA*, *calB*, *calC*, *calD*, *calE*, *calF*, *calG*, *calH*, *calI*, *calJ*, *calK*, *calL*, *calM*, *calN*, *calO*, *calP*, *calQ*, *calR*, *calS*, *calT*, *calU*, *calV*, *calW*, *calX*, *6MSAS*, *ActI*, *ActII*, *ActIII*, *orf1*, *orf2*, *orf3*, *orf4*, *orf5*, *orf6*, *orf7*, *orf8*, *orfI*, *orfII*, *orfIII*, *orfIV*, *orfV*, *orfVI*, *orfVII*, *orfVIII*, *orfIX*, *orfX*, *orfXI*, or an IS-element gene.
3. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes two or more proteins.
4. The isolated nucleic acid molecule of Claim 1, wherein said molecule comprises a complete nonchromoprotein enediyne biosynthetic gene cluster.
5. The isolated nucleic acid molecule of Claim 1, wherein said nonchromoprotein enediyne is calicheamicin.
6. An isolated nucleic acid molecule capable of hybridizing with a nucleic acid molecule from *Micromonospora echinospora* spp. *calichensis*, wherein said

nucleic acid molecule from *Micromonospora echinospora* spp. *calichensis* encodes one or more proteins from a nonchromoprotein enediyne biosynthetic gene cluster.

7. The isolated nucleic acid molecule of Claim 6, wherein said molecule encodes a protein having the activity of at least one protein from said nonchromoprotein enediyne biosynthetic gene cluster.
8. The isolated nucleic acid molecule of Claim 6, wherein said nucleic acid molecule comprises at least one of *calA*, *calB*, *calC*, *calD*, *calE*, *calF*, *calG*, *calH*, *calI*, *calJ*, *calK*, *calL*, *calM*, *calN*, *calO*, *calP*, *calQ*, *calR*, *calS*, *calT*, *calU*, *calV*, *calW*, *calX*, *6MSAS*, *ActI*, *ActII*, *ActIII*, *orf1*, *orf2*, *orf3*, *orf4*, *orf5*, *orf6*, *orf7*, *orf8*, *orfI*, *orfII*, *orfIII*, *orfIV*, *orfV*, *orfVI*, *orfVII*, *orfVIII*, *orfIX*, *orfX*, *orfXI* or an IS-element gene.
9. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.1.
10. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.3.
11. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.5.
12. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.7
13. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.9
14. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.11

15. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.13
16. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.15
17. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.17
18. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.19
19. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.21
20. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.23
21. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.25
22. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.27
23. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.29
24. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.31
25. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.33

26. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.35
27. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.37
28. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.39
29. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.41
30. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.43
31. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.45
32. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.47
33. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.49
34. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.51
35. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.53
36. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.55

37. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.57
38. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.59
39. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.61
40. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.63
41. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.65
42. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.67
43. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.69
44. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.71
45. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.73
46. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.75
47. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.77

48. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.79
49. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.81
50. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.83
51. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.85
52. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.87
53. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.89
54. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.91
55. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.93
56. The isolated nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises SEQ ID No.94
57. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a P<sub>450</sub> oxidase from *Micromonospora echinospora* spp. *calichensis*.

58. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a membrane transporter from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
59. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an *O*-methyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
60. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a glycosyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
61. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a *N,N*-dimethyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
62. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a dipeptide transporter from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
63. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a L-cysteine/cystine C-S-lyase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
64. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an oligopeptide transporter protein from a gene cluster of

*Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

65. The isolated nucleic acid molecule of Claim 1, which encodes a polypeptide encoding for a regulatory protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
66. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a hexopyranosyl-2-3-reductase from *Micromonospora echinospora* spp. *calichensis*.
67. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a desaturase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
68. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an UDP-D-glucose 6-dehydrogenase from *Micromonospora echinospora* spp. *calichensis*.
69. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a transcriptional regulator from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
70. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an oxygenase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.



71. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a halogenase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
72. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a  $\beta$ -keto-acyl synthase III from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
73. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a cytochrome P450 from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
74. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a TDP-4-keto-6-deoxy-L-hexose 2,3-dehydrogenase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
75. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an orsellenic acid synthase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
76. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a polyketide cyclase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

77. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a polyketide synthase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
78. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an integrase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
79. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a chromosome partitioning protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
80. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a hydroxylase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
81. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an aminotransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
82. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a glu-ammonia-ligase andenylyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
83. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a methyltransferase from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.

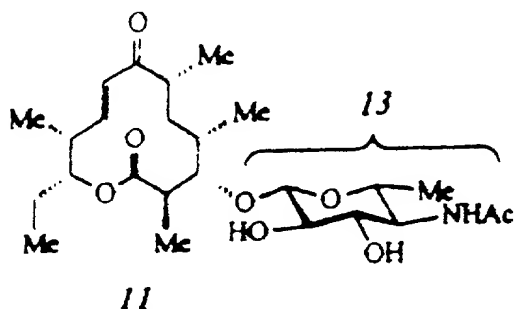
84. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an integral membrane protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
85. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes a membrane protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
86. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an immunity resistance protein from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
87. The isolated nucleic acid molecule of Claim 1, wherein said isolated nucleic acid molecule encodes an insertional element from a gene cluster of *Micromonospora echinospora* spp. *calichensis* coding for calicheamicin biosynthesis.
88. An expression vector comprising a nucleic acid molecule encoding a protein or biologically active fragment of a protein, wherein said nucleic acid molecule is a nucleic acid molecule of Claim 1.
89. The expression vector of Claim 88, wherein said nucleic acid molecule is operably linked to regulatory sequences to control expression of said protein or polypeptide.
90. The expression vector of Claim 89, wherein the regulatory sequence is a *Streptomyces* promoter.
91. A host cell transformed with the nucleic acid molecule of Claim 1.
92. A host cell transformed with the expression vector of Claim 88.

93. A host cell transformed with the expression vector of Claim 89.
94. The host cell of Claim 91, wherein said host cell is a bacterium, yeast, insect, plant, fungi, or mammalian cell.
95. The host cell of Claim 91, wherein the host bacteria is *E. coli* or *Streptomyces*.
96. A cosmid comprising an isolated nucleic acid molecule from a nonchromoprotein enediynes biosynthetic gene cluster from *Micromonospora echinospora*, wherein said isolated nucleic acid molecule comprises said nucleic acid molecule, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a protein or proteins, a portion or portions of said nucleic acid molecule wherein said portion or portions encode a biologically active fragment of a protein or proteins, a single-stranded nucleic acid molecule derived from said nucleic acid molecule, or a single-stranded nucleic acid molecule derived from a portion or portions of said nucleic acid molecule.
97. The cosmid of Claim 96, wherein said nucleic acid molecule comprises at least one of *calA*, *calB*, *calC*, *calD*, *calE*, *calF*, *calG*, *calH*, *calI*, *calJ*, *calK*, *calL*, *calM*, *calN*, *calO*, *calP*, *calQ*, *calR*, *calS*, *calT*, *calU*, *calV*, *calW*, *calX*, *6MSAS*, *ActI*, *ActII*, *ActIII*, *orf1*, *orf2*, *orf3*, *orf4*, *orf5*, *orf6*, *orf7*, *orf8*, *orfI*, *orfII*, *orfIII*, *orfIV*, *orfV*, *orfVI*, *orfVII*, *orfVIII*, *orfIX*, *orfX*, *orfXI* or an IS-element gene.
98. A method of expressing a protein comprising the steps of transfecting a host cell with the expression vector of Claim 88 and incubating said cell for a length of time and under conditions sufficient for expression of a desired quantity of said protein or said biologically active fragment of a protein.

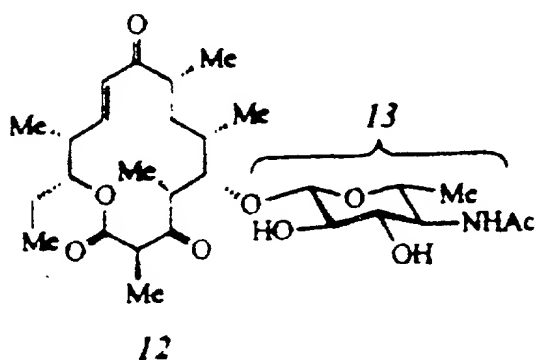
99. The method of Claim 97, wherein said host cell is a bacterium, yeast, insect, plant, fungi, or mammalian cell.
100. A method of purifying calicheamicin using affinity chromatography, comprising the steps of exposing a solution containing calicheamicin to an affinity column having CalC bound thereto, and recovering calicheamicin.
101. A polypeptide comprising amino acid sequence SEQ ID. No.: 2.
102. A polypeptide comprising amino acid sequence SEQ ID. No.: 4.
103. A polypeptide comprising amino acid sequence SEQ ID. No.: 6.
104. A polypeptide comprising amino acid sequence SEQ ID. No.: 8.
105. A polypeptide comprising amino acid sequence SEQ ID. No.: 10.
106. A polypeptide comprising amino acid sequence SEQ ID. No.: 12.
107. A polypeptide comprising amino acid sequence SEQ ID. No.: 14.
108. A polypeptide comprising amino acid sequence SEQ ID. No.: 16.
109. A polypeptide comprising amino acid sequence SEQ ID. No.: 18.
110. A polypeptide comprising amino acid sequence SEQ ID. No.: 20.
111. A polypeptide comprising amino acid sequence SEQ ID. No.: 22.
112. A polypeptide comprising amino acid sequence SEQ ID. No.: 24.
113. A polypeptide comprising amino acid sequence SEQ ID. No.: 26.
114. A polypeptide comprising amino acid sequence SEQ ID. No.: 28.
115. A polypeptide comprising amino acid sequence SEQ ID. No.: 30.
116. A polypeptide comprising amino acid sequence SEQ ID. No.: 32.
117. A polypeptide comprising amino acid sequence SEQ ID. No.: 34.
118. A polypeptide comprising amino acid sequence SEQ ID. No.: 36.

119. A polypeptide comprising amino acid sequence SEQ ID. No.: 38.
120. A polypeptide comprising amino acid sequence SEQ ID. No.: 40.
121. A polypeptide comprising amino acid sequence SEQ ID. No.: 42.
122. A polypeptide comprising amino acid sequence SEQ ID. No.: 44.
123. A polypeptide comprising amino acid sequence SEQ ID. No.: 46.
124. A polypeptide comprising amino acid sequence SEQ ID. No.: 48.
125. A polypeptide comprising amino acid sequence SEQ ID. No.: 50.
126. A polypeptide comprising amino acid sequence SEQ ID. No.: 52.
127. A polypeptide comprising amino acid sequence SEQ ID. No.: 54.
128. A polypeptide comprising amino acid sequence SEQ ID. No.: 58.
129. A polypeptide comprising amino acid sequence SEQ ID. No.: 60.
130. A polypeptide comprising amino acid sequence SEQ ID. No.: 62.
131. A polypeptide comprising amino acid sequence SEQ ID. No.: 64.
132. A polypeptide comprising amino acid sequence SEQ ID. No.: 66.
133. A polypeptide comprising amino acid sequence SEQ ID. No.: 68.
134. A polypeptide comprising amino acid sequence SEQ ID. No.: 80.
135. A polypeptide comprising amino acid sequence SEQ ID. No.: 82.
136. A polypeptide comprising amino acid sequence SEQ ID. No.: 84.
137. A polypeptide comprising amino acid sequence SEQ ID. No.: 86.
138. A polypeptide comprising amino acid sequence SEQ ID. No.: 88.
139. A polypeptide comprising amino acid sequence SEQ ID. No.: 90.
140. A polypeptide comprising amino acid sequence SEQ ID. No.: 92.
141. A polypeptide comprising amino acid sequence SEQ ID. No.: 95.

142. A method of conferring calicheamicin resistance on a subject comprising the steps of obtaining cells from the subject, transforming the cells with a calicheamicin self resistance gene, and returning the cells to the subject.
143. A compound having the structure:



144. A compound having the structure:



145. The isolated nucleic acid molecule of claim 1, wherein said protein comprises at least one of amino acid sequence SEQ ID Nos.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20,

22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95.

146. The isolated nucleic acid molecule of claim 1, wherein said biologically active fragment of a protein comprises a biologically active portion of at least one of amino acid sequence SEQ ID Nos.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95.
147. A polypeptide comprising amino acid sequence SEQ ID. No.: 56.
148. An isolated nucleic acid molecule comprising at least one of the nucleotide sequences of SEQ ID Nos. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, or 94, or a portion of portions thereof or an allele or alleles thereof, wherein said isolated nucleic acid molecule encodes a biologically functional protein or portion of a protein.
149. A polypeptide comprising the amino acid sequence of at least one of SEQ ID Nos. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, or 95, or a functional variant of one or more of those polypeptides.



## Abstract

An isolated gene cluster of *Micromonospora echinospora* which codes for calicheamicin biosynthesis. The biosynthetic gene cluster contains genes encoding proteins and enzymes used in the biosynthetic production of calicheamicin, including the aryltetrasaccharide and aglycone. The gene cluster also includes the gene coding for the protein conferring calicheamicin resistance. The invention also provides isolated genes of the biosynthetic cluster and their corresponding proteins. In addition, the invention relates to DNA hybridizing with the calicheamicin gene cluster and the isolated genes of that cluster. Expression vectors containing genes of the biosynthetic gene and their functional variants are also provided. The invention also relates to host cells conjugated with DNA isolated from the *Micromonospora echinospora* spp. *calichensis* genome.

Summary of cosmid clones isolated from *M. echinospora* genomic library.

clone <sup>a</sup>	type I PKS genes <sup>b</sup>	type II PKS genes <sup>b</sup>	deoxy sugar genes <sup>b</sup>	resistance ( $\mu\text{g mL}^{-1}$ ) <sup>c</sup>
3a	N.D. <sup>d</sup>	N.D. <sup>d</sup>	N.D. <sup>d</sup>	0.5
4a	N.D. <sup>d</sup>	N.D. <sup>d</sup>	N.D. <sup>d</sup>	0.5
4b	+	+	+	0.5
10a	+	+	+	0.5
13a	+	+	+	0.5
16a	N.D. <sup>d</sup>	N.D. <sup>d</sup>	N.D. <sup>d</sup>	0.5
56	+	+	+	0.1
58	-	-	+	< 0.01
60	+	+	+	0.05
66	-	-	+	0.04
puc18/pBluescript <sup>e</sup>	-	-	-	< 0.01

Fig. 1



Fig. 2

putative polypeptide	number of amino acids	proposed function or sequence similarity detected <sup>a</sup>	probability <sup>b</sup>	start/stop codons	best match
CalA	328	membrane transporter (ATP-binding)	$5.4 \times 10^{-124}$	ATG/TGA	DrrA <sup>97</sup>
CalB	561	membrane transporter	$5.5 \times 10^{-70}$	ATG/TGA	DrrB <sup>97</sup>
CalC	181	calicheamicin resistance protein	confirmed <sup>c</sup>	ATG/TGA	
CalD	263	O-methyltransferase	$1.1 \times 10^{-99}$	ATG/TGA	AveBVII <sup>98</sup>
CalE	420	Glycosyltransferase	$4.7 \times 10^{-30}$	GTG/TAG	EryCII <sup>99</sup>
CalF	245	N,N-dimethyltransferase	$1.5 \times 10^{-78}$	ATG/TGA	DesVI <sup>100</sup>
CalG	990	TDP-D-glucose 4,6-dehydratase	confirmed <sup>c</sup>	GTG/TAG	
CalH	338	Perosamine synthetase	confirmed <sup>c</sup>	GTG/TGA	
CalI	568	Dipeptide transporter	$1.7 \times 10^{-24}$	GTG/TGA	DciAE
CalJ	332	O-methyltransferase	$1.0 \times 10^{-37}$	ATG/TGA	DmpM
CalK	440	L-cysteine/cystine C-S-lyase	$1.6 \times 10^{-28}$	GTG/TGA	C-DES
CalL	562	Oligopeptide transporter protein	$9.5 \times 10^{-14}$	ATG/TGA	OppA
CalM	416	Regulatory protein		GTG/TGA	
CalN	398	Glycosyltransferase	$3.4 \times 10^{-79}$	ATG/TGA	OleI
CalO	331	Hexopyranosyl-2,3-reductase	$4.9 \times 10^{-139}$	ATG/TGA	EryBII
CalP	(179) <sup>d</sup>	Desaturase	$5.7 \times 10^{-7}$	/TGA	CrtI
CalQ	453	UDP-D-glucose 6-dehydrogenase	confirmed <sup>c</sup>	GTG/TGA	
CalR	282	Transcriptional regulator	$6.7 \times 10^{-11}$	ATG/TGA	SC5C7.03
CalS	1113	P <sub>450</sub> oxidase	$2.9 \times 10^{-66}$	GTG/TGA	BioI
CalT	432	oxygenase/halogenase	$2.0 \times 10^{-62}$	GTG/TAA	PCZA361.21
CalU	377	glycosyltransferase	$2.0 \times 10^{-53}$	ATG/TGA	SnogE/D
CalV	125	β-keto-acyl synthase III	$2.0 \times 10^{-65}$	ATG/TGA	SC4A9
CalW	(449) <sup>d</sup>	cytochrome P450	$1.0 \times 10^{-91}$	GTG/TGA	CYP105B1
CalX	(197) <sup>d</sup>	TDP-4-keto-6-deoxy-L-hexose 2,3-dehydratase	$1.0 \times 10^{-22}$	/TGA	MtmV
6MSAS	(198) <sup>d</sup>	orsellenic acid synthase	$6.5 \times 10^{-76}$	ATG/	AviM
ActI	(207) <sup>d</sup>	polyketide cyclase	$3.0 \times 10^{-66}$	/TGA	CurF
ActII	136	polyketide cyclase	$5.0 \times 10^{-53}$	ATG/TGA	SchB
ActIII	(308) <sup>d</sup>	polyketide synthase	$8.6 \times 10^{-148}$	GTG/	Pms1
orf1	322	unknown		ATG/TGA	
orf2	654	unknown		ATG/TGA	
orf3	373	integrase	$3.0 \times 10^{-13}$	ATG/TGA	Yld
orf4	521	chromosome partitioning protein	$3.3 \times 10^{-10}$	GTG/TAA	ParA
orf5	175	unknown		ATG/TGA	
orf6	139	unknown		ATG/TGA	
orf7	187	unknown		GTG/TGA	
orf8	266	regulatory protein	$3.0 \times 10^{-66}$	ATG/TGA	KorSA
OrfI	127	hydroxylase	$1.5 \times 10^{-7}$	ATG/TGA	SC4C6.24c
OrfII	248	unknown		GTG/TGA	
OrfIII	298	hydroxylase	$3.3 \times 10^{-90}$	GTG/TGA	SCA32
OrfIV	363	unknown	$5.3 \times 10^{-43}$	GTG/TGA	SC9C7.25
OrfV	288	aminotransferase	$2.9 \times 10^{-37}$	GTG/TGA	SCF55
OrfVI	1012	glu-ammonia-ligase adenyltransferase	exact	GTG/TGA	SCA32
OrfVII	236	Methyltransferase	$8.0 \times 10^{-63}$	GTG/TAG	SCF43A.25c
OrfVIII	441	Integral membrane protein	$8.9 \times 10^{-9}$	GTG/TGA	SCA32
OrfIX	478	Integral membrane protein	$1.1 \times 10^{-21}$	ATG/TGA	MLB268
OrfX	504	Membrane protein	$5.5 \times 10^{-20}$	GTG/TGA	B1496.F1.14
OrfXI	251	Immunity resistance protein	$1.1 \times 10^{-9}$	ATG/TGA	TFXG
IS-element	1209 bp	insertional element	$5.7 \times 10^{-168}$		IS1136 <sup>111</sup>

Fig.3.

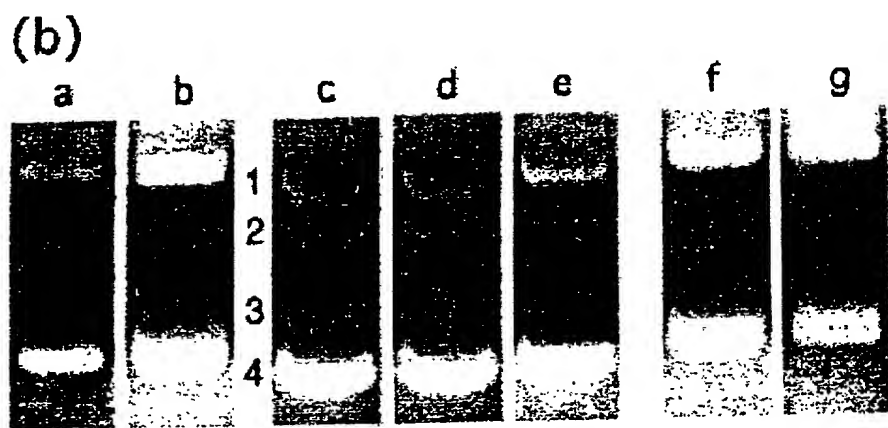
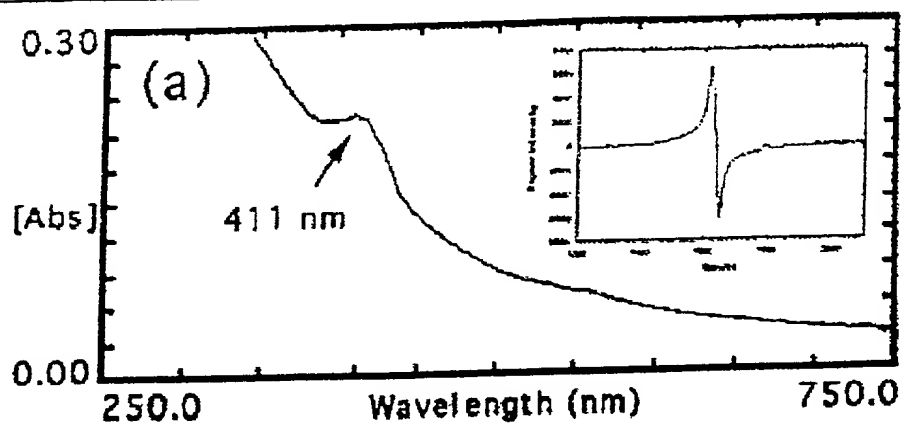


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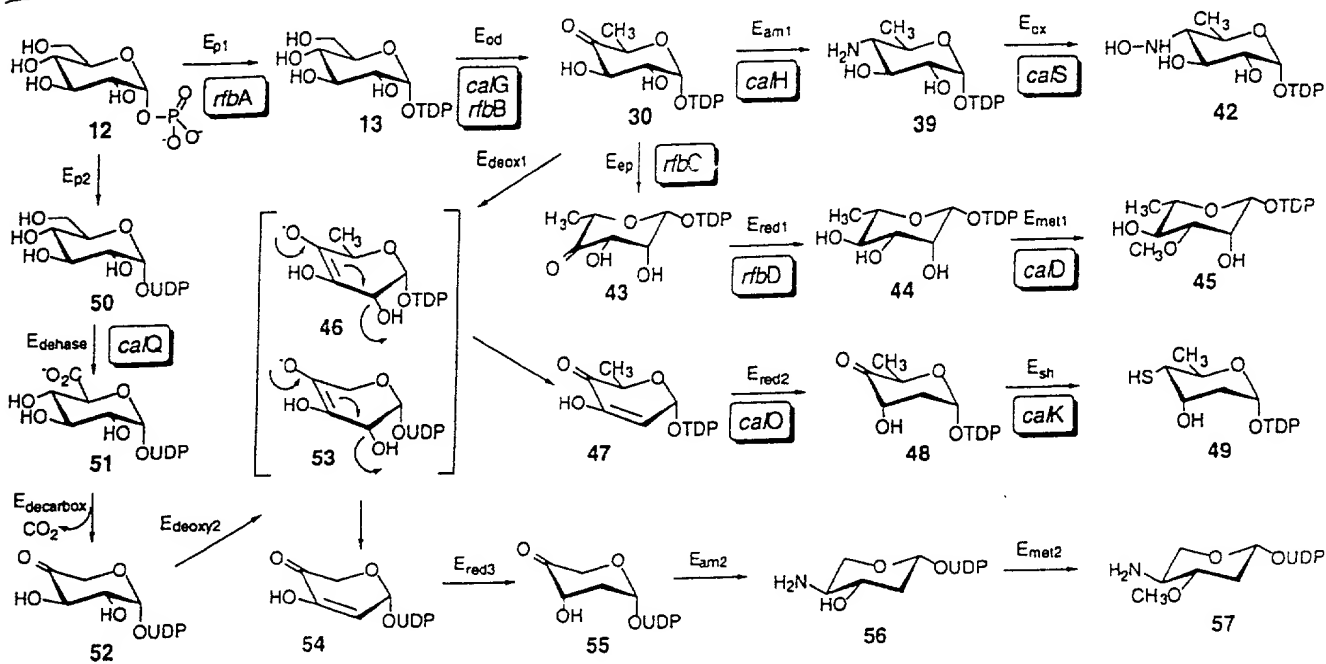


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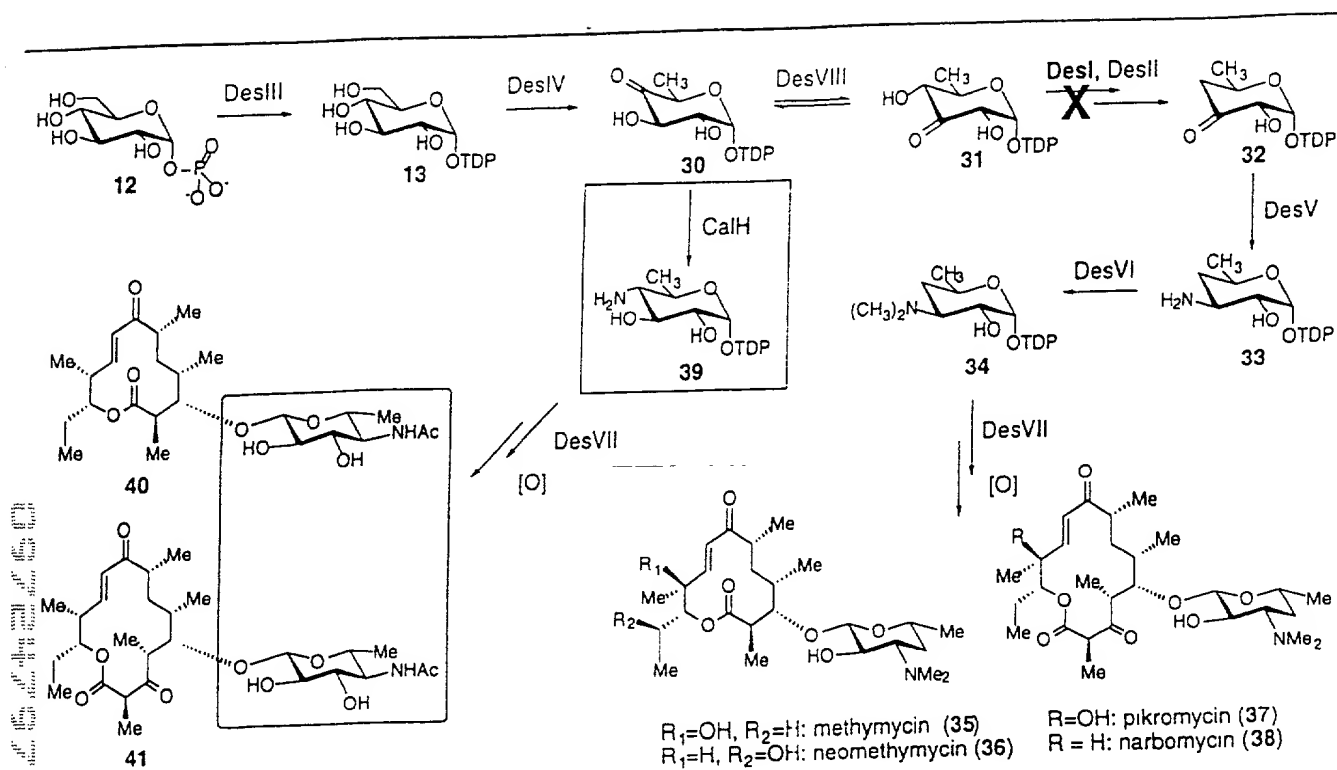
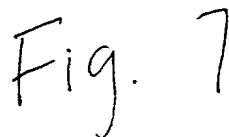


Fig. 6





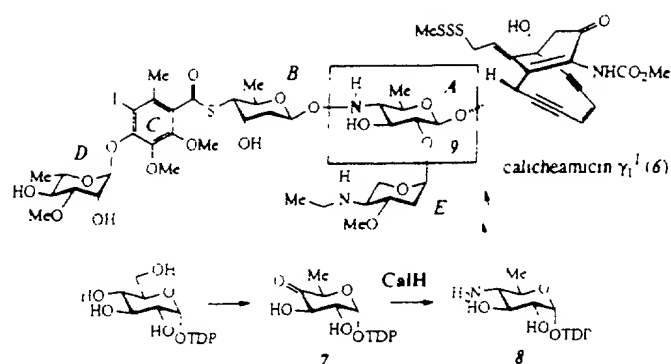
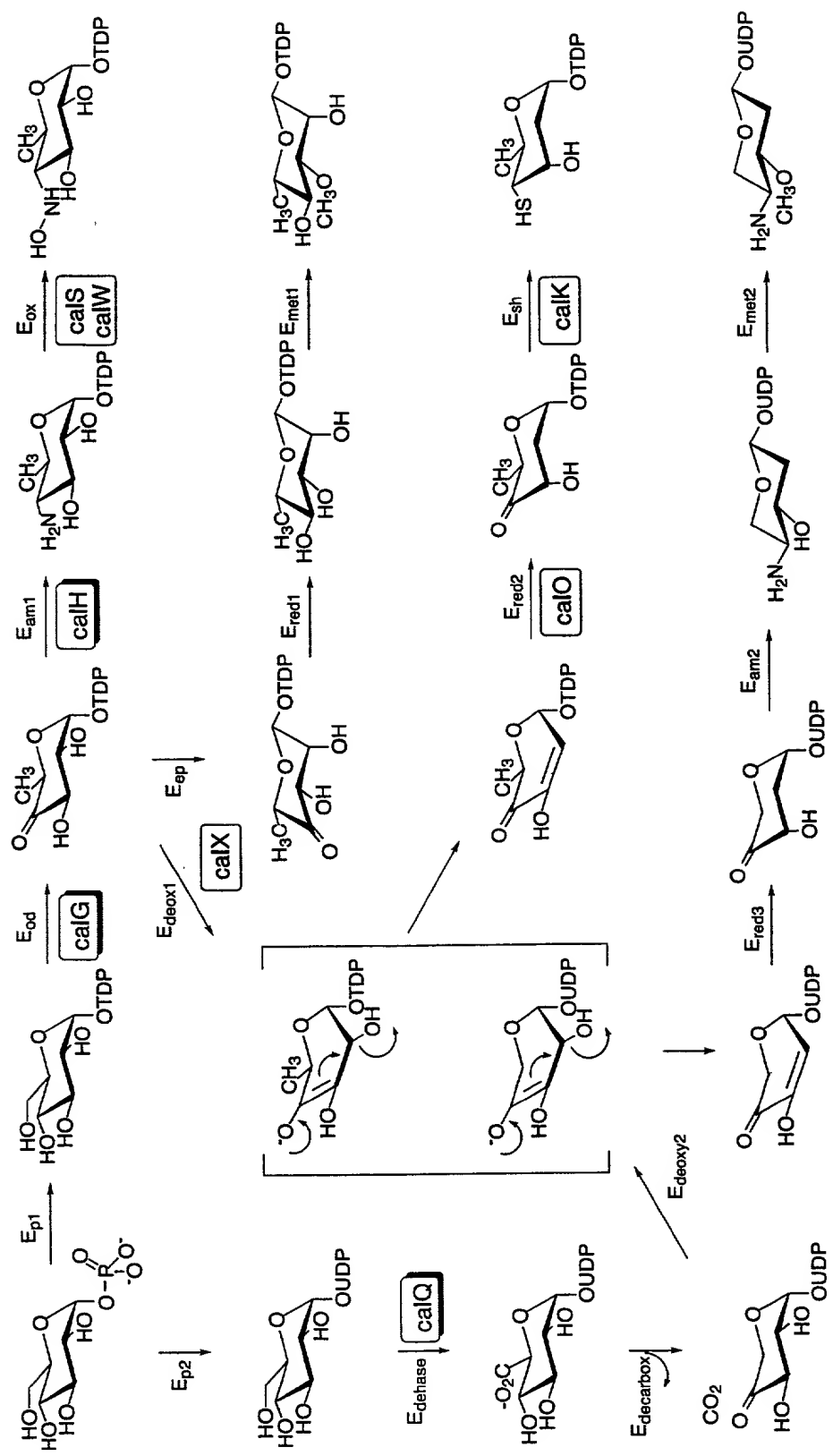


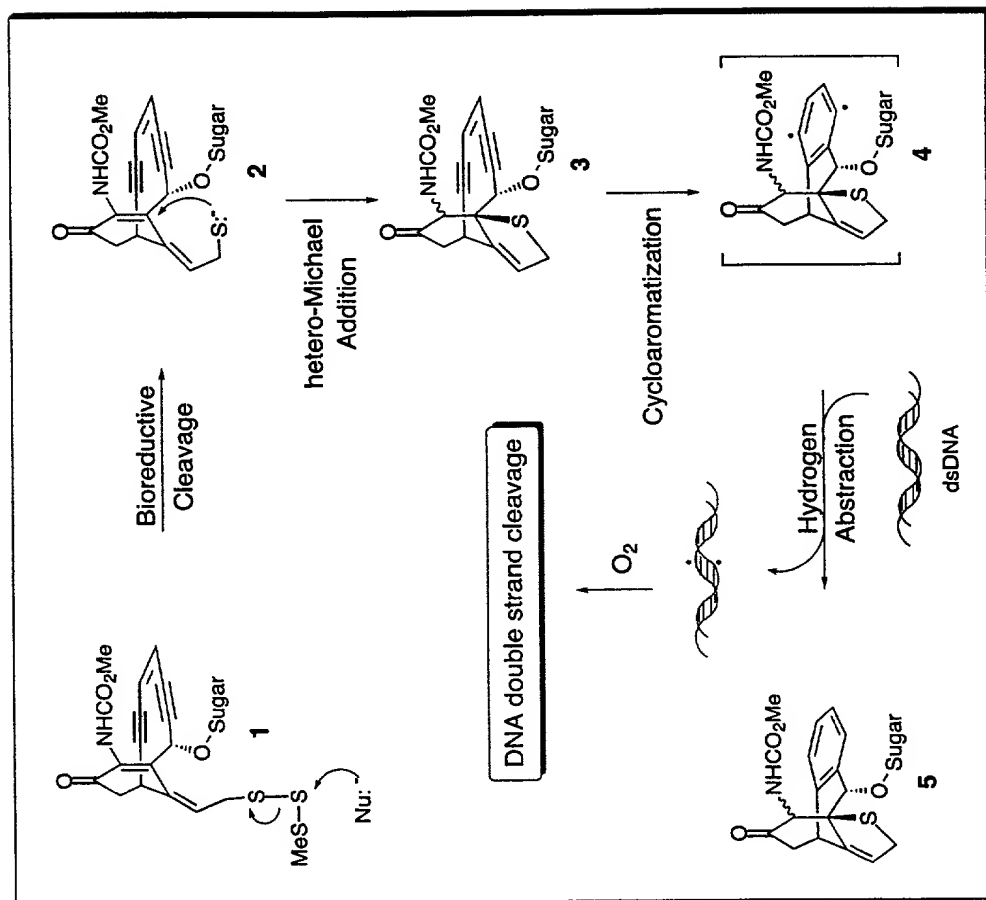
Fig. 8





105





8.  
#19

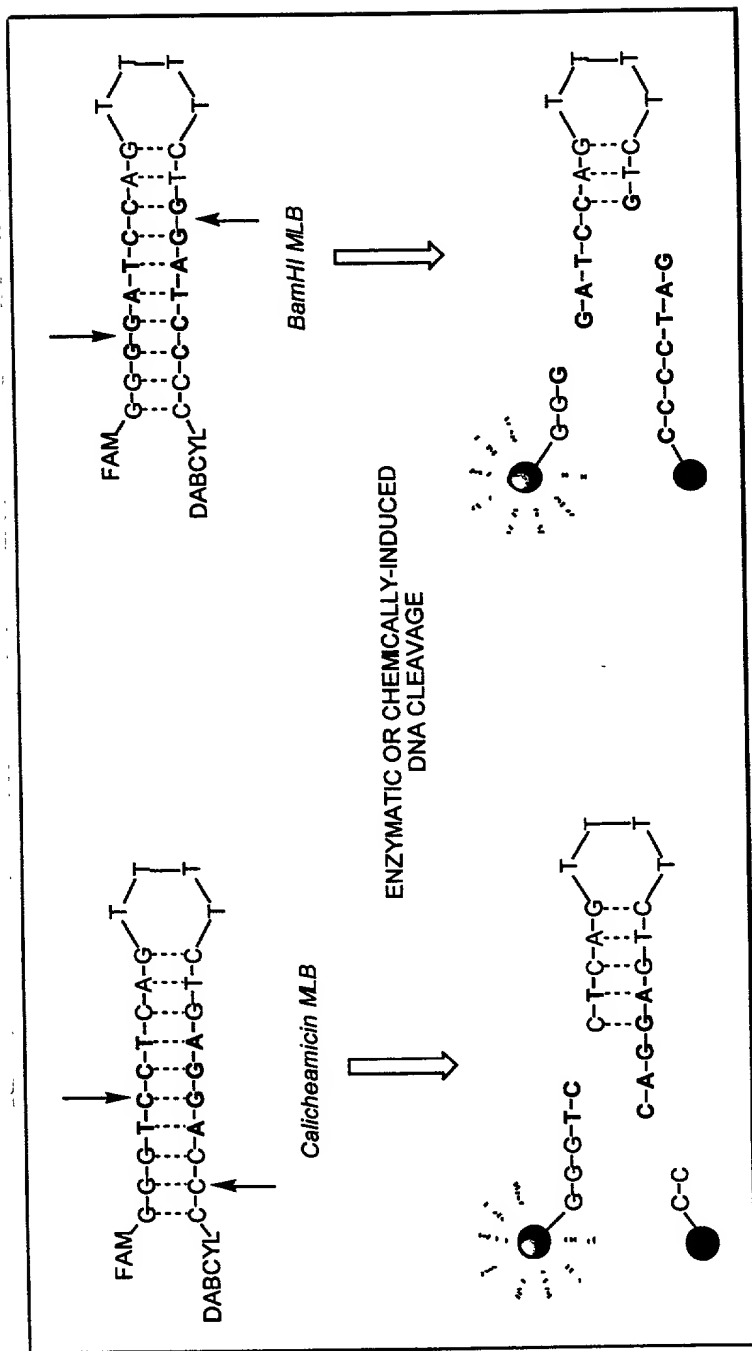


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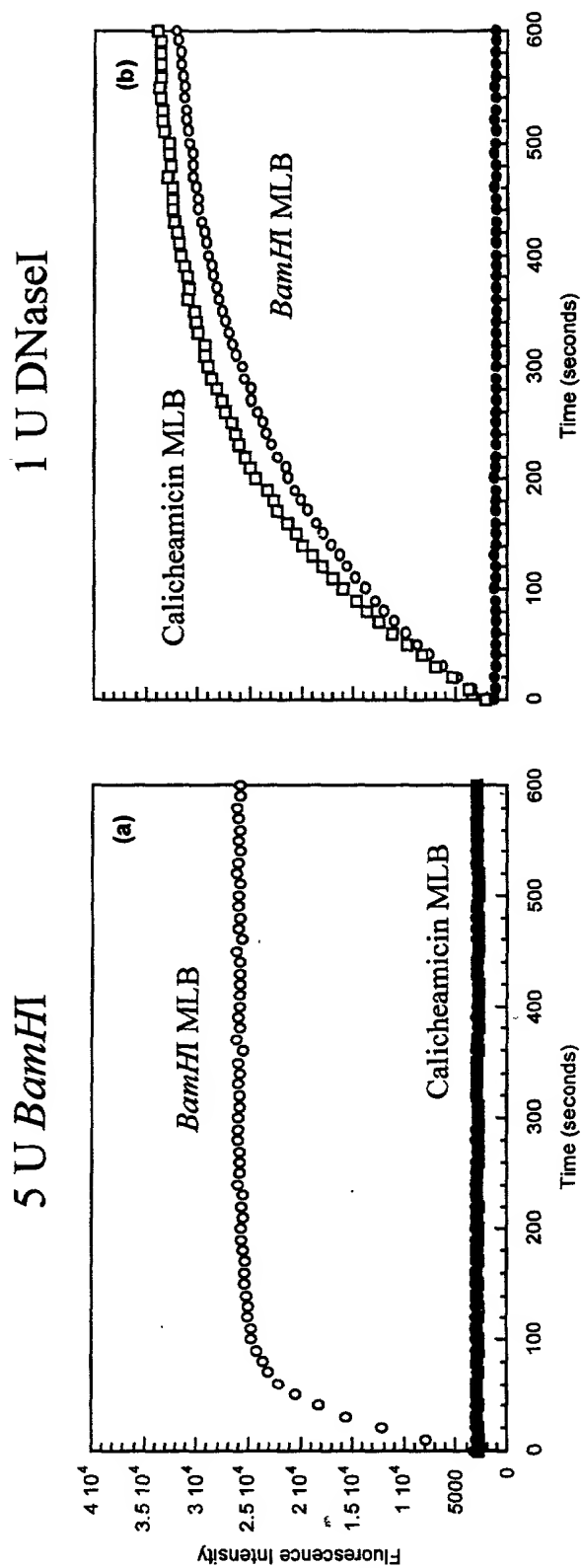


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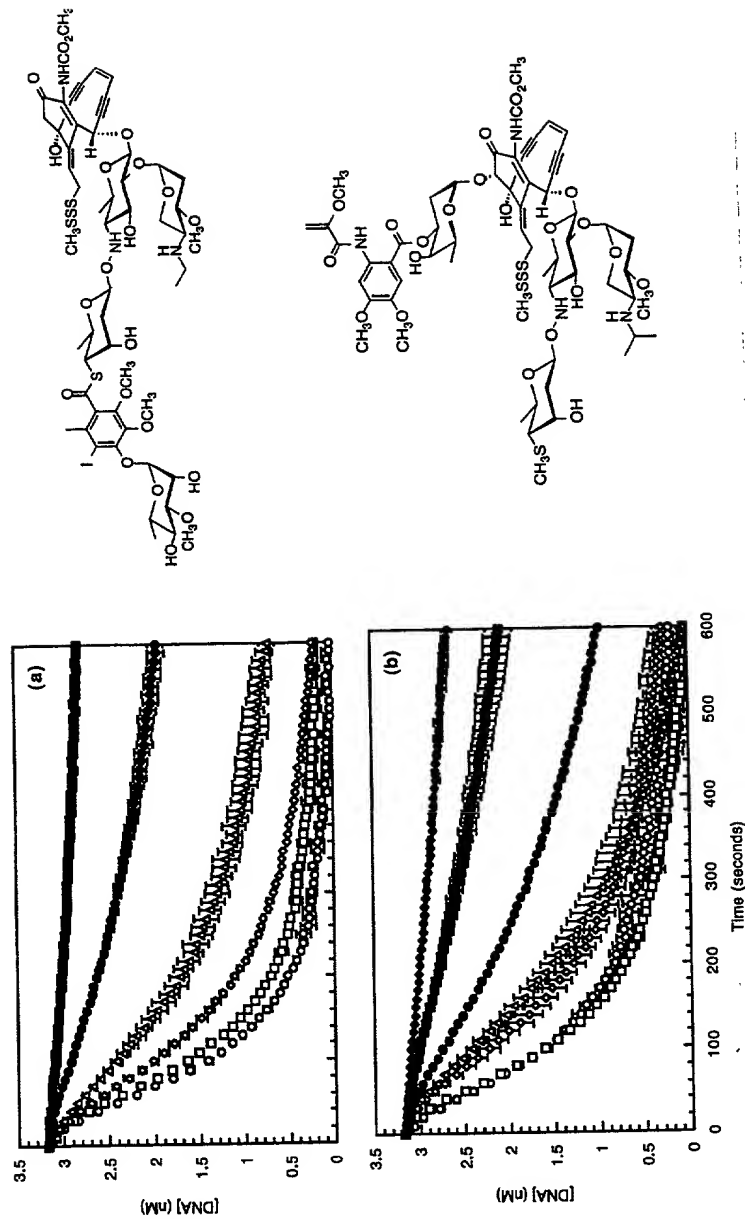


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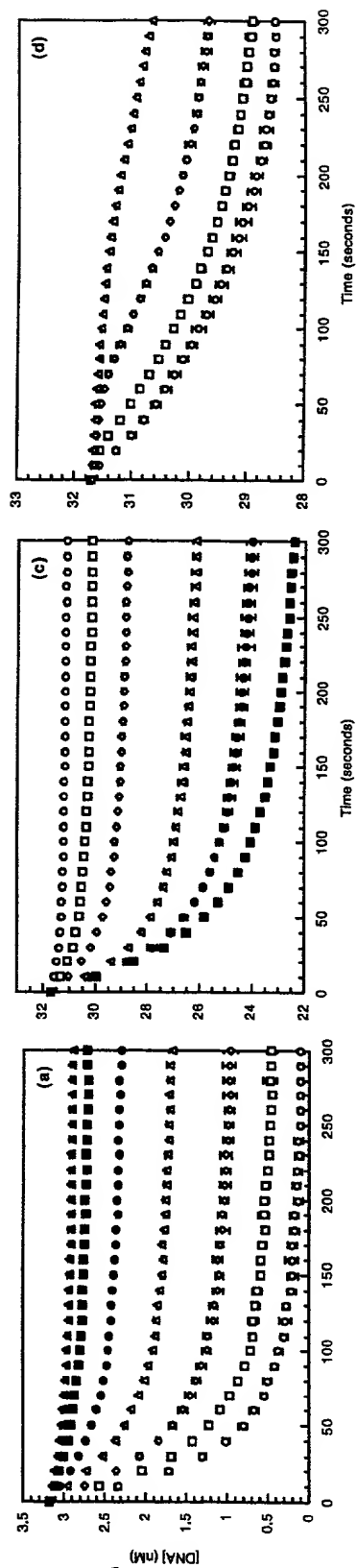
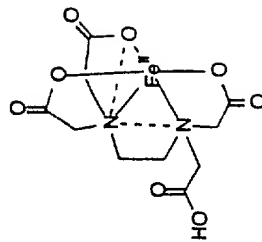
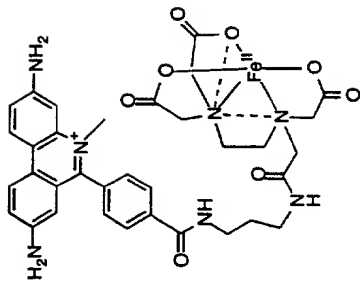
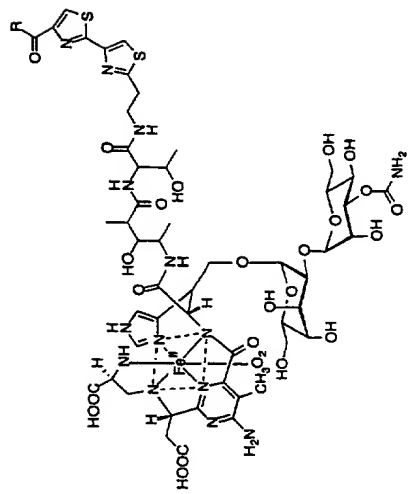
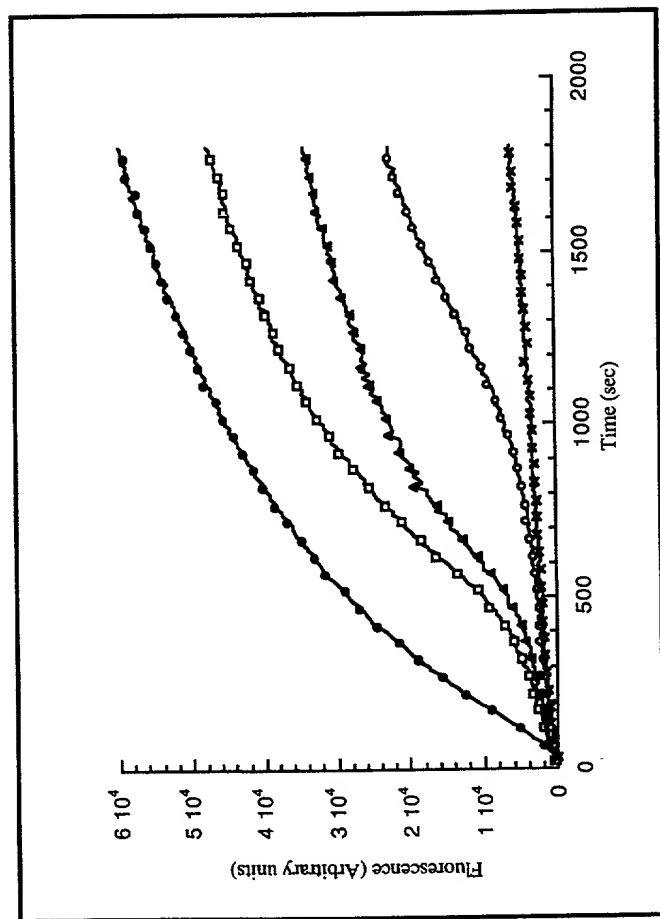


Fig 16



CalC (nmol)

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1.3  
2.6  
3.9  
5.2

Fig 17

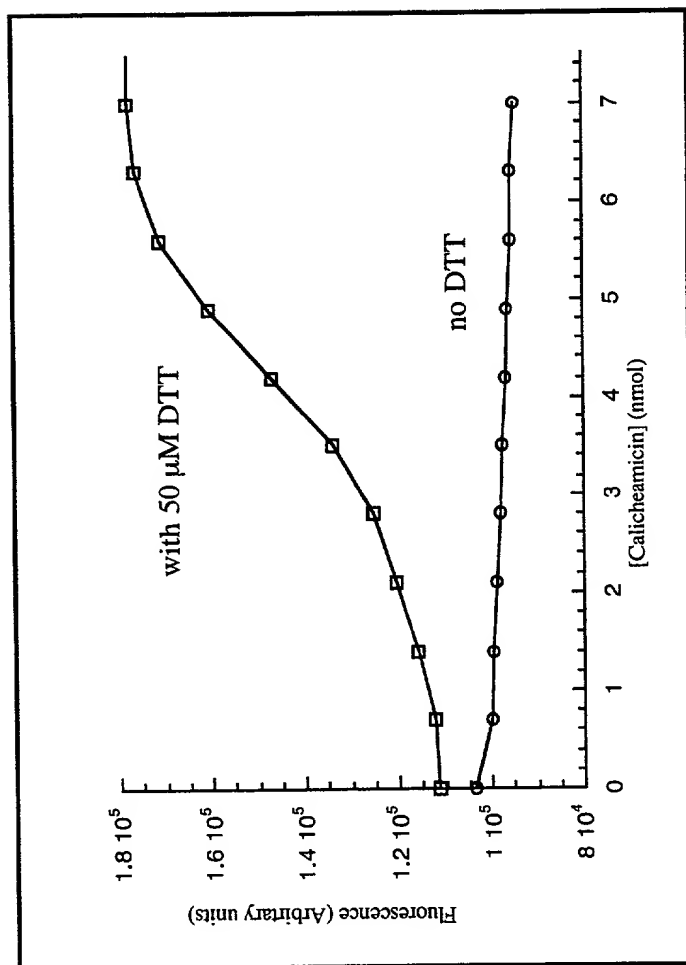
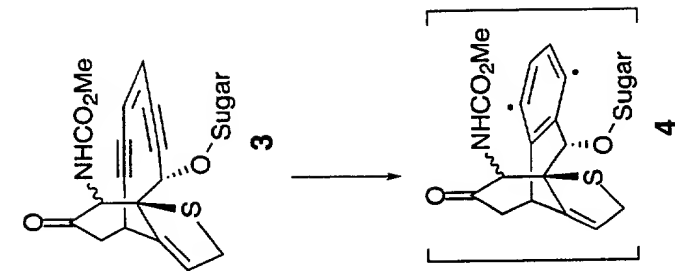


Fig 18

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<110> Jon S. THORSON

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ENCODING FOR BIOSYNTHESIS OF  
CALICHEAMICIN AND SELF-RESISTANCE THERETO

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agc	acc	gcc	gcg	aag	aag	ccg	aag	ccc	ccg	aac	tac	gac	ccg	ttc	gtc	96
Ser	Thr	Ala	Ala	Lys	Lys	Pro	Lys	Pro	Pro	Asn	Tyr	Asp	Pro	Phe	Val	
			20					25					30			

cgg	cac	agc	gtc	act	gtc	aag	gcc	gac	cgc	aag	acc	gcc	ttc	aag	acg	144
Arg	His	Ser	Val	Thr	Val	Lys	Ala	Asp	Arg	Lys	Thr	Ala	Phe	Lys	Thr	
		35					40					45				

ttc	ctc	gaa	ggc	ttt	ccg	gag	tgg	tgg	ccg	aac	aac	ttc	cgc	acc	acc	192
Phe	Leu	Glu	Gly	Phe	Pro	Glu	Trp	Trp	Pro	Asn	Asn	Phe	Arg	Thr	Thr	
	50					55					60					

aag	gtc	ggg	gcc	ccg	ctg	ggc	gtc	gac	aag	aag	ggc	ggc	cgc	tgg	tac	240
Lys	Val	Gly	Ala	Pro	Leu	Gly	Val	Asp	Lys	Lys	Gly	Gly	Arg	Trp	Tyr	
65					70					75				80		

gag	atc	gac	gag	cag	ggc	gag	gag	cac	acc	ttc	ggc	ctg	atc	cgg	aag	288
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			85					90						95		

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Gly Arg Ile Asp Pro Asp Asn Ser Ser Glu Phe Thr Val Thr Phe Val
      115      120      125

gcc gac ggc cag aag aag acc cgg gtg gac gtc gag cac acc cac ttc 432
Ala Asp Gly Gln Lys Lys Thr Arg Val Asp Val Glu His Thr His Phe
      130      135      140

gac cgg atg ggc acc aag cac gcc aag cgg gtc cgc aac ggc atg gac 480
Asp Arg Met Gly Thr Lys His Ala Lys Arg Val Arg Asn Gly Met Asp
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aag ggc tgg ccg acg atc ctc cag tcg ttc cag gac aag atc gac gag 528
Lys Gly Trp Pro Thr Ile Leu Gln Ser Phe Gln Asp Lys Ile Asp Glu
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 35      40      45
Phe Leu Glu Gly Phe Pro Glu Trp Trp Pro Asn Asn Phe Arg Thr Thr
 50      55      60
Lys Val Gly Ala Pro Leu Gly Val Asp Lys Lys Gly Gly Arg Trp Tyr
 65      70      75      80
Glu Ile Asp Glu Gln Gly Glu Glu His Thr Phe Gly Leu Ile Arg Lys
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Val Asp Glu Pro Asp Thr Leu Val Ile Gly Trp Arg Leu Asn Gly Phe
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Gly Arg Ile Asp Pro Asp Asn Ser Ser Glu Phe Thr Val Thr Phe Val
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Ala Asp Gly Gln Lys Lys Thr Arg Val Asp Val Glu His Thr His Phe
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Asp Arg Met Gly Thr Lys His Ala Lys Arg Val Arg Asn Gly Met Asp
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cgg ctg gag cac ggg ccg acc gtc gcc gag tac gag gcg gcc gtg ggc	144
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agt cgt atc ggc aac ccc ccg gtg gtc tcg gtc aac tgc ggc acg gcc	192
Ser Arg Ile Gly Asn Pro Arg Val Val Ser Val Asn Cys Gly Thr Ala	
50 55 60	
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Gly Leu His Leu Ala Leu Ser Leu Ala Ala Arg Pro Gly Ala Gly Glu	
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Ser Glu His Asp Gly Pro Gly Glu Val Leu Thr Thr Pro Leu Thr Phe	
85 90 95	
gag ggc acg aac tgg ccg atc ctc gcc aac ggg ctg cgc atc ccg tgg	336
Glu Gly Thr Asn Trp Pro Ile Leu Ala Asn Gly Leu Arg Ile Arg Trp	
100 105 110	
gtg gac gtc gac ccg gcc acc ctc aac atg gac ctc gac gac ctg gcc	384
Val Asp Val Asp Pro Ala Thr Leu Asn Met Asp Leu Asp Asp Leu Ala	
115 120 125	
gcg aag atc tcg ccc gcc acc ccg gcc atc gtg gtg gtc cac tgg ctc	432
Ala Lys Ile Ser Pro Ala Thr Arg Ala Ile Val Val Val His Trp Leu	
130 135 140	
ggc tac ccg gtg gac ctc aac ccg ctg cgc gcc gtc gtg gac ccg gcc	480
Gly Tyr Pro Val Asp Leu Asn Arg Leu Arg Ala Val Val Asp Arg Ala	
145 150 155 160	
acg gcg gga tac gac cgc cgc ccg ctg gtc gtg gag gac tgc gcg cag	528
Thr Ala Gly Tyr Asp Arg Arg Pro Leu Val Val Glu Asp Cys Ala Gln	
165 170 175	
gcg tgg ggc gcc acc tac ccg ggc gcg ccg ctg ggc acg cac ggc aac	576
Ala Trp Gly Ala Thr Tyr Arg Gly Ala Pro Leu Gly Thr His Gly Asn	
180 185 190	
gtc tgc gtg tac agc acc ggc gcg atc aag atc ctg acg acc ggc agc	624

Val Cys Val Tyr Ser Thr Gly Ala Ile Lys Ile Leu Thr Thr Gly Ser  
 195 200 205

ggc ggc ttc gtc gtg ctg ccc gac gac gac ctg tac gac cgg ctc cgg 672  
 Gly Gly Phe Val Val Leu Pro Asp Asp Asp Leu Tyr Asp Arg Leu Arg  
 210 215 220

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cgc cgg cac cgg gag aac gcc gcg ttc tac gac aag gaa ctg gcc ggc 864  
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Ser Arg Ile Gly Asn Pro Arg Val Val Ser Val Asn Cys Gly Thr Ala
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Gly Leu His Leu Ala Leu Ser Leu Ala Ala Arg Pro Gly Ala Gly Glu
65          70          75          80
Ser Glu His Asp Gly Pro Gly Glu Val Leu Thr Thr Pro Leu Thr Phe
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Glu Gly Thr Asn Trp Pro Ile Leu Ala Asn Gly Leu Arg Ile Arg Trp
          100          105          110
Val Asp Val Asp Pro Ala Thr Leu Asn Met Asp Leu Asp Asp Leu Ala
          115          120          125
Ala Lys Ile Ser Pro Ala Thr Arg Ala Ile Val Val Val His Trp Leu
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Gly Tyr Pro Val Asp Leu Asn Arg Leu Arg Ala Val Val Asp Arg Ala
145          150          155          160
Thr Ala Gly Tyr Asp Arg Arg Pro Leu Val Val Glu Asp Cys Ala Gln
          165          170          175
Ala Trp Gly Ala Thr Tyr Arg Gly Ala Pro Leu Gly Thr His Gly Asn
          180          185          190
Val Cys Val Tyr Ser Thr Gly Ala Ile Lys Ile Leu Thr Thr Gly Ser
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Gly Gly Phe Val Val Leu Pro Asp Asp Asp Leu Tyr Asp Arg Leu Arg
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Leu Arg Arg Trp Leu Gly Ile Glu Arg Ala Ser Asp Arg Ile Thr Gly
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Asp Tyr Asp Val Ala Glu Trp Gly Tyr Arg Phe Ile Leu Asn Glu Ile
          245          250          255
Gly Gly Ala Ile Gly Leu Ser Asn Leu Glu Arg Val Asp Glu Leu Leu
          260          265          270
Arg Arg His Arg Glu Asn Ala Ala Phe Tyr Asp Lys Glu Leu Ala Gly
          275          280          285
Ile Asp Gly Val Glu Gln Thr Glu Arg Ala Asp Asp Arg Glu Pro Ala
290          295          300
Phe Trp Met Tyr Pro Leu Lys Val Arg Asp Arg Pro Ala Phe Met Arg
305          310          315          320
Arg Leu Leu Asp Ala Gly Ile Ala Thr Ser Val Val Ser Arg Arg Asn
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Asp Ala His Ser Cys Val Ala Ser Ala Arg Thr Thr Leu Pro Gly Leu
          340          345          350
Asp Arg Val Ala Asp Arg Val Val His Ile Pro Val Gly Trp Trp Leu
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Val	Val	Glu	Arg	Leu	Val	Arg	Arg	Gly	Asp	Glu	Val	Val	Val	Tyr	Asp	
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ctc	gcc	gac	ccg	ccg	ccc	gac	ctg	gag	cac	ccg	ccg	ggc	gcg	atc	cgg	144
Leu	Ala	Asp	Pro	Pro	Pro	Asp	Leu	Glu	His	Pro	Pro	Gly	Ala	Ile	Arg	
		35					40					45				

cac	gtc	cgc	ggc	gac	gtc	cgg	gac	gcc	gac	ggg	ctg	gcg	gcc	gcc	gcc	192
His	Val	Arg	Gly	Asp	Val	Arg	Asp	Ala	Asp	Gly	Leu	Ala	Ala	Ala	Ala	
	50					55				60						

acc	ggc	gtg	gac	gag	gtc	tac	cac	ctc	gcg	gcg	gtc	gtc	ggc	gtc	gac	240
Thr	Gly	Val	Asp	Glu	Val	Tyr	His	Leu	Ala	Ala	Val	Val	Gly	Val	Asp	
65					70				75					80		

cgg	tac	ctc	agc	cgg	ccg	ctg	gac	gtg	gtc	gag	atc	aac	gtg	gac	ggc	288
Arg	Tyr	Leu	Ser	Arg	Pro	Leu	Asp	Val	Val	Glu	Ile	Asn	Val	Asp	Gly	
			85					90					95			

acc	cgg	aac	gcg	ttg	cgc	gcc	gca	ctg	cgc	gcc	ggg	gcc	cgg	gtc	gtg	336
Thr	Arg	Asn	Ala	Leu	Arg	Ala	Ala	Leu	Arg	Ala	Gly	Ala	Arg	Val	Val	
		100					105					110				

gtg	tcc	agc	acc	agc	gag	gtg	tac	ggg	cgc	aat	ccg	cgg	gtg	ccg	tgg	384
Val	Ser	Ser	Thr	Ser	Glu	Val	Tyr	Gly	Arg	Asn	Pro	Arg	Val	Pro	Trp	

115	120	125	
cgg gag gac gac gac cgg gtg ctc ggc agc acg gcg acg gac cgg tgg			432
Arg Glu Asp Asp Asp Arg Val Leu Gly Ser Thr Ala Thr Asp Arg Trp			
130	135	140	
tcg tac tcg acg agc aag gcg gcg gcc gag cac ctg gcc ttc gcc ttc			480
Ser Tyr Ser Thr Ser Lys Ala Ala Ala Glu His Leu Ala Phe Ala Phe			
145	150	155	160
cac cgg cag gag ggc ctg ccg gtg acg gtg ctg cgg tac ttc aac gtc			528
His Arg Gln Glu Gly Leu Pro Val Thr Val Leu Arg Tyr Phe Asn Val			
	165	170	175
tac ggc cca cgc cag cgc ccg gcg tac gtc ctc agc cgc acc gtc gcc			576
Tyr Gly Pro Arg Gln Arg Pro Ala Tyr Val Leu Ser Arg Thr Val Ala			
	180	185	190
cgc ctg ctg cgg ggc gtt ccg ccc gtg gtg tac gac gac ggc cgc cag			624
Arg Leu Leu Arg Gly Val Pro Pro Val Val Tyr Asp Asp Gly Arg Gln			
	195	200	205
acg cgg tgc ttc acc tgg atc gac gag gcg gcc gag gcg acc ctg ctg			672
Thr Arg Cys Phe Thr Trp Ile Asp Glu Ala Ala Glu Ala Thr Leu Leu			
	210	215	220
gcc gcc gcc cac ccg cgg gcc gtc ggc gag tgt ttc aac atc ggc agc			720
Ala Ala Ala His Pro Arg Ala Val Gly Glu Cys Phe Asn Ile Gly Ser			
	225	230	235
agc gtg gag acc acc gtc gcc gag gcg gtc cgg ctg gcc ggc acg gtg			768
Ser Val Glu Thr Thr Val Ala Glu Ala Val Arg Leu Ala Gly Thr Val			
	245	250	255
gcc ggg gtg ccg gtg gcg gcc cag acc gcg gac acc gga gcc ggg ctc			816
Ala Gly Val Pro Val Ala Ala Gln Thr Ala Asp Thr Gly Ala Gly Leu			
	260	265	270
ggc gcc cgc tac cag gac att ccc cgc cgc gta ccg gac tgc ggc aag			864
Gly Ala Arg Tyr Gln Asp Ile Pro Arg Arg Val Pro Asp Cys Gly Lys			
	275	280	285
gcc gcc gcg ctg ctg gac tgg cgg gcc cgg gtg ccg ctg gtg acc ggc			912
Ala Ala Ala Leu Leu Asp Trp Arg Ala Arg Val Pro Leu Val Thr Gly			
	290	295	300
ctg cgc cgg acc gtc gag tgg gcc cgc cgc aac ccg tgg tgg acc gcc			960
Leu Arg Arg Thr Val Glu Trp Ala Arg Arg Asn Pro Trp Trp Thr Ala			
	305	310	315
cag gcc gac gac gga ctg gtc gtc agg tag			990
Gln Ala Asp Asp Gly Leu Val Val Arg *			
	325		

<210> 6

<211> 329

<212> PRT

<213> Bacteria

<400> 6

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Met Pro Arg Ser Leu Val Thr Gly Gly Phe Gly Phe Val Gly Ser His
 1          5          10          15
Val Val Glu Arg Leu Val Arg Arg Gly Asp Glu Val Val Val Tyr Asp
          20          25          30
Leu Ala Asp Pro Pro Pro Asp Leu Glu His Pro Pro Gly Ala Ile Arg
          35          40          45
His Val Arg Gly Asp Val Arg Asp Ala Asp Gly Leu Ala Ala Ala Ala
          50          55          60
Thr Gly Val Asp Glu Val Tyr His Leu Ala Ala Val Val Gly Val Asp
65          70          75          80
Arg Tyr Leu Ser Arg Pro Leu Asp Val Val Glu Ile Asn Val Asp Gly
          85          90          95
Thr Arg Asn Ala Leu Arg Ala Ala Leu Arg Ala Gly Ala Arg Val Val
          100          105          110
Val Ser Ser Thr Ser Glu Val Tyr Gly Arg Asn Pro Arg Val Pro Trp
          115          120          125
Arg Glu Asp Asp Asp Arg Val Leu Gly Ser Thr Ala Thr Asp Arg Trp
          130          135          140
Ser Tyr Ser Thr Ser Lys Ala Ala Ala Glu His Leu Ala Phe Ala Phe
145          150          155          160
His Arg Gln Glu Gly Leu Pro Val Thr Val Leu Arg Tyr Phe Asn Val
          165          170          175
Tyr Gly Pro Arg Gln Arg Pro Ala Tyr Val Leu Ser Arg Thr Val Ala
          180          185          190
Arg Leu Leu Arg Gly Val Pro Pro Val Val Tyr Asp Asp Gly Arg Gln
          195          200          205
Thr Arg Cys Phe Thr Trp Ile Asp Glu Ala Ala Glu Ala Thr Leu Leu
          210          215          220
Ala Ala Ala His Pro Arg Ala Val Gly Glu Cys Phe Asn Ile Gly Ser
225          230          235          240
Ser Val Glu Thr Thr Val Ala Glu Ala Val Arg Leu Ala Gly Thr Val
          245          250          255
Ala Gly Val Pro Val Ala Ala Gln Thr Ala Asp Thr Gly Ala Gly Leu
          260          265          270
Gly Ala Arg Tyr Gln Asp Ile Pro Arg Arg Val Pro Asp Cys Gly Lys
          275          280          285
Ala Ala Ala Leu Leu Asp Trp Arg Ala Arg Val Pro Leu Val Thr Gly
          290          295          300
Leu Arg Arg Thr Val Glu Trp Ala Arg Arg Asn Pro Trp Trp Thr Ala
305          310          315          320
Gln Ala Asp Asp Gly Leu Val Val Arg
          325
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<210> 7

<211> 987

<212> DNA

<213> Bacteria

<220>

<221> CDS

<222> (1) ... (987)

<400> 7

atg aca acc aat ccg gcc ttg gcc atc gag acc cgc gat ctg gtg aag 48

Met	Thr	Thr	Asn	Pro	Ala	Leu	Ala	Ile	Glu	Thr	Arg	Asp	Leu	Val	Lys	
1				5					10					15		
gtc ttc ggc cag acg cgc gcg gtc gac gga ctg gac ctg gtg gtg cgg 96																
Val	Phe	Gly	Gln	Thr	Arg	Ala	Val	Asp	Gly	Leu	Asp	Leu	Val	Val	Arg	
			20					25					30			
gcc ggg acg atc cac ggg gtg ctg ggc ccg aac ggc gcc ggc aag acg 144																
Ala	Gly	Thr	Ile	His	Gly	Val	Leu	Gly	Pro	Asn	Gly	Ala	Gly	Lys	Thr	
			35				40					45				
acg gcc atc aag atg ctc gcc acg ctg atg cga ccc acc tcc ggc acc 192																
Thr	Ala	Ile	Lys	Met	Leu	Ala	Thr	Leu	Met	Arg	Pro	Thr	Ser	Gly	Thr	
			50				55				60					
gcg tcc gtg ctg ggg cac gac gtg gtc cgc gag gcc gcc gag gtc cgg 240																
Ala	Ser	Val	Leu	Gly	His	Asp	Val	Val	Arg	Glu	Ala	Ala	Glu	Val	Arg	
	65				70				75					80		
cgc cgc atc ggc ctc acc ggc cag acc atg tcc gtc gac gag gac atg 288																
Arg	Arg	Ile	Gly	Leu	Thr	Gly	Gln	Thr	Met	Ser	Val	Asp	Glu	Asp	Met	
			85					90					95			
acc ggc gtg cag aac ctg atc ctc gcc ggc cgc ctg cag ggt ctg cgg 336																
Thr	Gly	Val	Gln	Asn	Leu	Ile	Leu	Ala	Gly	Arg	Leu	Gln	Gly	Leu	Arg	
			100					105					110			
cac gcg tcc gcg gcc gcg cgg gcg gag cag ttg atg gag gcg ttc gac 384																
His	Ala	Ser	Ala	Ala	Ala	Arg	Ala	Glu	Gln	Leu	Met	Glu	Ala	Phe	Asp	
			115				120					125				
ctc acc gag gtc ggc ggc cgg ctg gtg aag acc ttc tcc ggc ggc cag 432																
Leu	Thr	Glu	Val	Gly	Gly	Arg	Leu	Val	Lys	Thr	Phe	Ser	Gly	Gly	Gln	
			130				135				140					
cgg cgg cgc atc gac gtg gcc gcg agc atg gtg gtc acc ccc gag ctg 480																
Arg	Arg	Arg	Ile	Asp	Val	Ala	Ala	Ser	Met	Val	Val	Thr	Pro	Glu	Leu	
				150					155					160		
ctg ttc ctc gac gag ccg acc acc ggc ctc gac ccg cgc agc cgc agc 528																
Leu	Phe	Leu	Asp	Glu	Pro	Thr	Thr	Gly	Leu	Asp	Pro	Arg	Ser	Arg	Ser	
			165					170						175		
gag gtc tgg gag atg atc cgg gcg ctg gtc cgg gac ggg ggc acc gtc 576																
Glu	Val	Trp	Glu	Met	Ile	Arg	Ala	Leu	Val	Arg	Asp	Gly	Gly	Thr	Val	
			180					185					190			
ctg ctg acc acg cag tac ctc gac gag gcg gac cac ctc gcc gac gag 624																
Leu	Leu	Thr	Thr	Gln	Tyr	Leu	Asp	Glu	Ala	Asp	His	Leu	Ala	Asp	Glu	
			195				200					205				
ctg acg ctc atc gac cac ggc cgc atc gtg gcg cag ggc acc ccg ccg 672																
Leu	Thr	Leu	Ile	Asp	His	Gly	Arg	Ile	Val	Ala	Gln	Gly	Thr	Pro	Pro	
			210				215				220					
gag ctg aag gcg agc cgc gcc gcc ggc gtg ctc gac gtg cgg ctg cgt 720																
Glu	Leu	Lys	Ala	Ser	Arg	Ala	Ala	Gly	Val	Leu	Asp	Val	Arg	Leu	Arg	
				230					235					240		

```

gac ccc gag cgc cgg gcc gac gcg ggc gcc ctg ctc gcc aag gcc gtc 768
Asp Pro Glu Arg Arg Ala Asp Ala Gly Ala Leu Leu Ala Lys Ala Val
                245                250                255

ggc gcc gcc gcc gac ctc gac tcc gat ccg gcg cgg ctg tcg gtg cgg 816
Gly Ala Ala Ala Asp Leu Asp Ser Asp Pro Ala Arg Leu Ser Val Arg
                260                265                270

gtg acc gac ccc gac cgg gcg gcg ctg gcc ctg ggc gag ctg gcg cgg 864
Val Thr Asp Pro Asp Arg Ala Ala Leu Ala Leu Gly Glu Leu Ala Arg
                275                280                285

gcc ggc atc cac gtc gac gac ttc acg ctc ggc cag ccc tcg ctc gac 912
Ala Gly Ile His Val Asp Asp Phe Thr Leu Gly Gln Pro Ser Leu Asp
                290                295                300

acg gtg ttc ctc gcc ctc acc ggt cac tcg acg gtc gac gcc agc gaa 960
Thr Val Phe Leu Ala Leu Thr Gly His Ser Thr Val Asp Ala Ser Glu
305                310                315                320

gaa gag gaa gca gag gta cgg gca tga 987
Glu Glu Glu Ala Glu Val Arg Ala *
                325

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<210> 8
<211> 328
<212> PRT
<213> Bacteria

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<400> 8
Met Thr Thr Asn Pro Ala Leu Ala Ile Glu Thr Arg Asp Leu Val Lys
 1          5          10          15
Val Phe Gly Gln Thr Arg Ala Val Asp Gly Leu Asp Leu Val Val Arg
 20          25          30
Ala Gly Thr Ile His Gly Val Leu Gly Pro Asn Gly Ala Gly Lys Thr
 35          40          45
Thr Ala Ile Lys Met Leu Ala Thr Leu Met Arg Pro Thr Ser Gly Thr
 50          55          60
Ala Ser Val Leu Gly His Asp Val Val Arg Glu Ala Ala Glu Val Arg
 65          70          75          80
Arg Arg Ile Gly Leu Thr Gly Gln Thr Met Ser Val Asp Glu Asp Met
 85          90          95
Thr Gly Val Gln Asn Leu Ile Leu Ala Gly Arg Leu Gln Gly Leu Arg
100          105          110
His Ala Ser Ala Ala Ala Arg Ala Glu Gln Leu Met Glu Ala Phe Asp
115          120          125
Leu Thr Glu Val Gly Gly Arg Leu Val Lys Thr Phe Ser Gly Gly Gln
130          135          140
Arg Arg Arg Ile Asp Val Ala Ala Ser Met Val Val Thr Pro Glu Leu
145          150          155          160
Leu Phe Leu Asp Glu Pro Thr Thr Gly Leu Asp Pro Arg Ser Arg Ser
165          170          175
Glu Val Trp Glu Met Ile Arg Ala Leu Val Arg Asp Gly Gly Thr Val
180          185          190
Leu Leu Thr Thr Gln Tyr Leu Asp Glu Ala Asp His Leu Ala Asp Glu
195          200          205

```



Leu Thr Leu Ile Asp His Gly Arg Ile Val Ala Gln Gly Thr Pro Pro  
 210 215 220  
 Glu Leu Lys Ala Ser Arg Ala Ala Gly Val Leu Asp Val Arg Leu Arg  
 225 230 235 240  
 Asp Pro Glu Arg Arg Ala Asp Ala Gly Ala Leu Leu Ala Lys Ala Val  
 245 250 255  
 Gly Ala Ala Ala Asp Leu Asp Ser Asp Pro Ala Arg Leu Ser Val Arg  
 260 265 270  
 Val Thr Asp Pro Asp Arg Ala Ala Leu Ala Leu Gly Glu Leu Ala Arg  
 275 280 285  
 Ala Gly Ile His Val Asp Asp Phe Thr Leu Gly Gln Pro Ser Leu Asp  
 290 295 300  
 Thr Val Phe Leu Ala Leu Thr Gly His Ser Thr Val Asp Ala Ser Glu  
 305 310 315 320  
 Glu Glu Glu Ala Glu Val Arg Ala  
 325

<210> 9  
 <211> 1686  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> misc\_feature  
 <222> (1)...(1686)  
 <223> n = A,T,C or G

<221> misc\_feature  
 <222> (1)...(1686)  
 <223> n = A,T,C or G

<221> CDS  
 <222> (1)...(1686)

<400> 9  
 atg acg aca ccc agc acc gag gtg cgg ccg ctg ccg gcc gag atc ttc 48  
 Met Thr Thr Pro Ser Thr Glu Val Arg Pro Leu Pro Ala Glu Ile Phe  
 1 5 10 15  
 agc cga tcg gtg gcc ggc gcg gaa cgg ccg cca cgc ccc ggc ccg ctg 96  
 Ser Arg Ser Val Ala Gly Ala Glu Arg Pro Pro Arg Pro Gly Pro Leu  
 20 25 30  
 ttc gcc gtc cgc acc ttc gcc tgg cgg aac ctg atc aag ctc cgg tac 144  
 Phe Ala Val Arg Thr Phe Ala Trp Arg Asn Leu Ile Lys Leu Arg Tyr  
 35 40 45  
 gtg cag gac cac ctg ggc acc gcg gtg gtc ttc ccg atc atc ctg acg 192  
 Val Gln Asp His Leu Gly Thr Ala Val Val Phe Pro Ile Ile Leu Thr  
 50 55 60  
 ctg gtc ttc acc tat ctg ctc ggc ggc gcg atc gcc ggc tcg ccc cgg 240  
 Leu Val Phe Thr Tyr Leu Leu Gly Gly Ala Ile Ala Gly Ser Pro Arg  
 65 70 75 80  
 gag tac ctg cag ttc ttc ctt ccc ggc gtg atc gtc ctc tcg ctc gtg 288  
 Glu Tyr Leu Gln Phe Phe Leu Pro Gly Val Ile Val Leu Ser Leu Val

	85	90	95	
tcg tcg agc atg atg agc gcc ctg acg ctg aac cgg gac atc gcc acc				336
Ser Ser Ser Met Met Ser Ala Leu Thr Leu Asn Arg Asp Ile Ala Thr				
	100	105	110	
ggc atg ttc gac cgg gtc cgc agc acg ccc atc tgg cag ccc gcg gta				384
Gly Met Phe Asp Arg Val Arg Ser Thr Pro Ile Trp Gln Pro Ala Val				
	115	120	125	
ctg gtc ggg gcg atg gcc ggc gac gcc gtc cgg tac gcc ctg acc tcg				432
Leu Val Gly Ala Met Ala Gly Asp Ala Val Arg Tyr Ala Leu Thr Ser				
	130	135	140	
atc gtg ccg ctg tcg ctc ggc ctg ctg ctc ggc ttc cgg ccg gac ggc				480
Ile Val Pro Leu Ser Leu Gly Leu Leu Leu Gly Phe Arg Pro Asp Gly				
	145	150	155	160
ggc ctg tcc ggg gtg gtg ctc gcc ctg ctc tac ctg cag ctg ttc acc				528
Gly Leu Ser Gly Val Val Leu Ala Leu Leu Tyr Leu Gln Leu Phe Thr				
	165	170	175	
ttc agc gtc gcc tgg ctg tgg atg ctg ttc gcg gtg ctg atc ccg cag				576
Phe Ser Val Ala Trp Leu Trp Met Leu Phe Ala Val Leu Ile Pro Gln				
	180	185	190	
ccg acc gcc gcc gcc ggc gtg gtg aac ctc ctg cag ttc gtg ctc ctc				624
Pro Thr Ala Ala Ala Gly Val Val Asn Leu Leu Gln Phe Val Leu Leu				
	195	200	205	
ttc ggc agc aac atc ctg gcg ccg tcg cag acg atg ccg ggc tgg ctg				672
Phe Gly Ser Asn Ile Leu Ala Pro Ser Gln Thr Met Pro Gly Trp Leu				
	210	215	220	
gag gcg gtg gtc aag ttg aac ccc gtc acc cac gcc gcg acc gcc acc				720
Glu Ala Val Val Lys Leu Asn Pro Val Thr His Ala Ala Thr Ala Thr				
	225	230	235	240
cgc ggg ctg ntg cac ggc acg gtg acc tcg ggg gag atg ggc gcn ggc				768
Arg Gly Leu Xaa His Gly Thr Val Thr Ser Gly Glu Met Gly Ala Gly				
	245	250	255	
ctg ctg acc tgc gcc gtg ctc atc gtg gct gct cgc ccc gcc cac gat				816
Leu Leu Thr Cys Ala Val Leu Ile Val Ala Ala Arg Pro Ala His Asp				
	260	265	270	
ctg gct cta cag ccg caa gca gcg ctg aca ccc ctc ccc gac ggc ccc				864
Leu Ala Leu Gln Pro Gln Ala Ala Leu Thr Pro Leu Pro Asp Gly Pro				
	275	280	285	
ggg gtg ccc cct gtt ctc ctc gca ggg gca ggc ccg ggg ccg tcg ccg				912
Gly Val Pro Pro Val Leu Leu Ala Gly Ala Gly Pro Gly Pro Ser Arg				
	290	295	300	
cat ccc gcc gcc ggt ccg cgc tgt gcc ccg gcc gca ccc gga gcc ttt				960
His Pro Ala Ala Gly Arg Arg Cys Ala Pro Ala Ala Pro Gly Ala Phe				
	305	310	315	320

gcc gcg ccg gcc acc gct gct gcg gcc gta acc gcc cgc tgt gtc ggt 1008  
Ala Ala Pro Ala Thr Ala Ala Ala Val Thr Ala Arg Cys Val Gly  
325 330 335

cac cgg cgc cgt ggc ggc gca ccg tgt cgg ggc cgg ctg ccc act tgt 1056  
His Arg Arg Arg Gly Gly Ala Pro Cys Arg Gly Arg Leu Pro Thr Cys  
340 345 350

ggc cgc cgt gcg gtc ggc gga cgg acg gcg gcc ccg gac gga cat gag 1104  
Gly Arg Arg Ala Val Gly Gly Arg Thr Ala Ala Pro Asp Gly His Glu  
355 360 365

tcc gtc cgg ggc cgc gtc gtg gtc ggt cga gca gct ccc gac cgg cta 1152  
Ser Val Arg Gly Arg Val Val Val Gly Arg Ala Ala Pro Asp Arg Leu  
370 375 380

cga gcc gga gtg gac cag cgc ggc cca ggc ctc gcc gcg ctc ctg cga 1200  
Arg Ala Gly Val Asp Gln Arg Gly Pro Gly Leu Ala Ala Leu Leu Arg  
385 390 395 400

gat ccg cat cat ctc ggg gct cgg ctc gaa ctc ctc ggc cgc gtc ctc 1248  
Asp Pro His His Leu Gly Ala Arg Leu Glu Leu Leu Gly Arg Val Leu  
405 410 415

cgg gac cgg gcc gcc cgg cag gtc gcc ccg gat gaa cat acc gag gaa 1296  
Arg Asp Arg Ala Ala Arg Gln Val Ala Pro Asp Glu His Thr Glu Glu  
420 425 430

gtc gag cgc cat ctc cca gcc gac gcc gac ctc cac gag cat ctg ctc 1344  
Val Glu Arg His Leu Pro Ala Asp Ala Asp Leu His Glu His Leu Leu  
435 440 445

cga ggt cgt ggc gtg ctc cag ctc cag cag ggt gcc gtc gcc ctc ctc 1392  
Arg Gly Arg Gly Val Leu Gln Leu Gln Gln Gly Ala Val Ala Leu Leu  
450 455 460

gtc agc cgc agc tcc acc tcg ctg tcc ggc ttg ccc tcg tac acc cag 1440  
Val Ser Arg Ser Ser Thr Ser Leu Ser Gly Leu Pro Ser Tyr Thr Gln  
465 470 475 480

ctg atg gtg agc cgg cgc ggt ggc tcg cag cgc agg atg tcg ccg ctg 1488  
Leu Met Val Ser Arg Arg Gly Gly Ser Gln Arg Arg Met Ser Pro Leu  
485 490 495

gcg ttg ccc tgc agg gcg aag ttg cca ccc tcg cgg agg tcg ccc ttg 1536  
Ala Leu Pro Cys Arg Ala Lys Leu Pro Pro Ser Arg Arg Ser Pro Leu  
500 505 510

ggc tcg atg aac cag cgg ttg atg cgg ttc ggg tcg gtg cag gcg ctc 1584  
Gly Ser Met Asn Gln Arg Leu Met Arg Phe Gly Ser Val Gln Ala Leu  
515 520 525

cag acc tcg tcg acg ggc gcg tcg tac cgt tgc cgg atg atg atg ctg 1632  
Gln Thr Ser Ser Thr Gly Ala Ser Tyr Arg Cys Arg Met Met Met Leu  
530 535 540

cgg gcc tcg ccg gcc ggg atg gtg cgc cgg ccg agg gca cgc tcc gtc 1680  
Arg Ala Ser Pro Ala Gly Met Val Arg Arg Pro Arg Ala Arg Ser Val

545

550

555

560

gcc tga  
Ala \*

1686

<210> 10  
<211> 561  
<212> PRT  
<213> Bacteria

<220>  
<221> VARIANT  
<222> (1)...(561)  
<223> Xaa = Any Amino Acid

<221> VARIANT  
<222> (1)...(561)  
<223> Xaa = Any Amino Acid

<400> 10  
Met Thr Thr Pro Ser Thr Glu Val Arg Pro Leu Pro Ala Glu Ile Phe  
1 5 10 15  
Ser Arg Ser Val Ala Gly Ala Glu Arg Pro Pro Arg Pro Gly Pro Leu  
20 25 30  
Phe Ala Val Arg Thr Phe Ala Trp Arg Asn Leu Ile Lys Leu Arg Tyr  
35 40 45  
Val Gln Asp His Leu Gly Thr Ala Val Val Phe Pro Ile Ile Leu Thr  
50 55 60  
Leu Val Phe Thr Tyr Leu Leu Gly Gly Ala Ile Ala Gly Ser Pro Arg  
65 70 75 80  
Glu Tyr Leu Gln Phe Phe Leu Pro Gly Val Ile Val Leu Ser Leu Val  
85 90 95  
Ser Ser Ser Met Met Ser Ala Leu Thr Leu Asn Arg Asp Ile Ala Thr  
100 105 110  
Gly Met Phe Asp Arg Val Arg Ser Thr Pro Ile Trp Gln Pro Ala Val  
115 120 125  
Leu Val Gly Ala Met Ala Gly Asp Ala Val Arg Tyr Ala Leu Thr Ser  
130 135 140  
Ile Val Pro Leu Ser Leu Gly Leu Leu Leu Gly Phe Arg Pro Asp Gly  
145 150 155 160  
Gly Leu Ser Gly Val Val Leu Ala Leu Leu Tyr Leu Gln Leu Phe Thr  
165 170 175  
Phe Ser Val Ala Trp Leu Trp Met Leu Phe Ala Val Leu Ile Pro Gln  
180 185 190  
Pro Thr Ala Ala Ala Gly Val Val Asn Leu Leu Gln Phe Val Leu Leu  
195 200 205  
Phe Gly Ser Asn Ile Leu Ala Pro Ser Gln Thr Met Pro Gly Trp Leu  
210 215 220  
Glu Ala Val Val Lys Leu Asn Pro Val Thr His Ala Ala Thr Ala Thr  
225 230 235 240  
Arg Gly Leu Xaa His Gly Thr Val Thr Ser Gly Glu Met Gly Ala Gly  
245 250 255  
Leu Leu Thr Cys Ala Val Leu Ile Val Ala Ala Arg Pro Ala His Asp  
260 265 270  
Leu Ala Leu Gln Pro Gln Ala Ala Leu Thr Pro Leu Pro Asp Gly Pro  
275 280 285

Gly Val Pro Pro Val Leu Leu Ala Gly Ala Gly Pro Gly Pro Ser Arg  
 290 295 300  
 His Pro Ala Ala Gly Arg Arg Cys Ala Pro Ala Ala Pro Gly Ala Phe  
 305 310 315 320  
 Ala Ala Pro Ala Thr Ala Ala Ala Val Thr Ala Arg Cys Val Gly  
 325 330 335  
 His Arg Arg Arg Gly Gly Ala Pro Cys Arg Gly Arg Leu Pro Thr Cys  
 340 345 350  
 Gly Arg Arg Ala Val Gly Gly Arg Thr Ala Ala Pro Asp Gly His Glu  
 355 360 365  
 Ser Val Arg Gly Arg Val Val Val Gly Arg Ala Ala Pro Asp Arg Leu  
 370 375 380  
 Arg Ala Gly Val Asp Gln Arg Gly Pro Gly Leu Ala Ala Leu Leu Arg  
 385 390 395 400  
 Asp Pro His His Leu Gly Ala Arg Leu Glu Leu Leu Gly Arg Val Leu  
 405 410 415  
 Arg Asp Arg Ala Ala Arg Gln Val Ala Pro Asp Glu His Thr Glu Glu  
 420 425 430  
 Val Glu Arg His Leu Pro Ala Asp Ala Asp Leu His Glu His Leu Leu  
 435 440 445  
 Arg Gly Arg Gly Val Leu Gln Leu Gln Gln Gly Ala Val Ala Leu Leu  
 450 455 460  
 Val Ser Arg Ser Ser Thr Ser Leu Ser Gly Leu Pro Ser Tyr Thr Gln  
 465 470 475 480  
 Leu Met Val Ser Arg Arg Gly Gly Ser Gln Arg Arg Met Ser Pro Leu  
 485 490 495  
 Ala Leu Pro Cys Arg Ala Lys Leu Pro Pro Ser Arg Arg Ser Pro Leu  
 500 505 510  
 Gly Ser Met Asn Gln Arg Leu Met Arg Phe Gly Ser Val Gln Ala Leu  
 515 520 525  
 Gln Thr Ser Ser Thr Gly Ala Ser Tyr Arg Cys Arg Met Met Met Leu  
 530 535 540  
 Arg Ala Ser Pro Ala Gly Met Val Arg Arg Pro Arg Ala Arg Ser Val  
 545 550 555 560  
 Ala

<210> 11  
 <211> 792  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1) ... (792)

<400> 11  
 atg cga tgg agg ctg cgg atg gac agc ggc gac ggt cag gac ctg cgt 48  
 Met Arg Trp Arg Leu Arg Met Asp Ser Gly Asp Gly Gln Asp Leu Arg  
 1 5 10 15  
 gcg ttc gtg cac gac tca ccg gag gag acg gag acc acc cag cgc ctg 96  
 Ala Phe Val His Asp Ser Pro Glu Glu Thr Glu Thr Thr Gln Arg Leu  
 20 25 30  
 acg aag ctc ttg acc aac tct ccg atc ccc acg gag gaa ctg gtc aac 144  
 Thr Lys Leu Leu Thr Asn Ser Pro Ile Pro Thr Glu Glu Leu Val Asn

35	40	45	
aac ctc ccc ctg ttc ctg cgc cgc cac cag atg acc gat ctg ctc tcg			192
Asn Leu Pro Leu Phe Leu Arg Arg His Gln Met Thr Asp Leu Leu Ser			
50	55	60	
atg gac gcg ctc tac cgt cag gtc ctc gac gtg ccg ggc gtg atc atg			240
Met Asp Ala Leu Tyr Arg Gln Val Leu Asp Val Pro Gly Val Ile Met			
65	70	75	80
gag ttc ggc gtc cgg ttc ggc cgt cac ctc ggc acg ttc gcc gcc ctg			288
Glu Phe Gly Val Arg Phe Gly Arg His Leu Gly Thr Phe Ala Ala Leu			
85	90	95	
cgc ggt gtc tac gag ccc tac aac ccg ctg cgc cgc atc gtc ggc ttc			336
Arg Gly Val Tyr Glu Pro Tyr Asn Pro Leu Arg Arg Ile Val Gly Phe			
100	105	110	
gac acc ttc acc ggc ttc ccc gac gtc aac gac gtc gac cgc gtc ggc			384
Asp Thr Phe Thr Gly Phe Pro Asp Val Asn Asp Val Asp Arg Val Gly			
115	120	125	
ccc acg gcg tac cag ggc cgc ttc gca gtg ccc ggg ggc tat ccg gcg			432
Pro Thr Ala Tyr Gln Gly Arg Phe Ala Val Pro Gly Gly Tyr Pro Ala			
130	135	140	
tac ctg aaa gag gtg ctg gac gcg cac gag tgc agc gac ttc ttc ggc			480
Tyr Leu Lys Glu Val Leu Asp Ala His Glu Cys Ser Asp Phe Phe Gly			
145	150	155	160
cac gtg acg cag cgc agc gtg ctc gtc gag ggg gac gta cgg gag acg			528
His Val Thr Gln Arg Ser Val Leu Val Glu Gly Asp Val Arg Glu Thr			
165	170	175	
gtg ccg cgc tac ctc gcg gag aac ccg cag acc gtc atc gcg ctg gcg			576
Val Pro Arg Tyr Leu Ala Glu Asn Pro Gln Thr Val Ile Ala Leu Ala			
180	185	190	
tac ttc gac ctc gac ctc tac gag ccg acg aag gcc gtc ctg gag gcg			624
Tyr Phe Asp Leu Asp Leu Tyr Glu Pro Thr Lys Ala Val Leu Glu Ala			
195	200	205	
atc cgc ccc tac ctc acc aag ggc agc atc gtc gcc ttc gac gaa ctc			672
Ile Arg Pro Tyr Leu Thr Lys Gly Ser Ile Val Ala Phe Asp Glu Leu			
210	215	220	
gac aat ccg aag tgg ccc ggc gag aac atc gcg atg ccg aag gtg ctc			720
Asp Asn Pro Lys Trp Pro Gly Glu Asn Ile Ala Met Arg Lys Val Leu			
225	230	235	240
ggg ctg gac cac gcc ccg ctg cgc ctg ctg ccg ggc cgc ccg gcg ccg			768
Gly Leu Asp His Ala Pro Leu Arg Leu Leu Pro Gly Arg Pro Ala Pro			
245	250	255	
gcg tac ctg cgg tgg ggc gac tga			792
Ala Tyr Leu Arg Trp Gly Asp *			
260			

<210> 12  
 <211> 263  
 <212> PRT  
 <213> Bacteria

<400> 12

Met	Arg	Trp	Arg	Leu	Arg	Met	Asp	Ser	Gly	Asp	Gly	Gln	Asp	Leu	Arg
1				5					10					15	
Ala	Phe	Val	His	Asp	Ser	Pro	Glu	Glu	Thr	Glu	Thr	Thr	Gln	Arg	Leu
			20					25					30		
Thr	Lys	Leu	Leu	Thr	Asn	Ser	Pro	Ile	Pro	Thr	Glu	Glu	Leu	Val	Asn
		35					40					45			
Asn	Leu	Pro	Leu	Phe	Leu	Arg	Arg	His	Gln	Met	Thr	Asp	Leu	Leu	Ser
	50					55				60					
Met	Asp	Ala	Leu	Tyr	Arg	Gln	Val	Leu	Asp	Val	Pro	Gly	Val	Ile	Met
65					70					75				80	
Glu	Phe	Gly	Val	Arg	Phe	Gly	Arg	His	Leu	Gly	Thr	Phe	Ala	Ala	Leu
				85					90					95	
Arg	Gly	Val	Tyr	Glu	Pro	Tyr	Asn	Pro	Leu	Arg	Arg	Ile	Val	Gly	Phe
			100					105					110		
Asp	Thr	Phe	Thr	Gly	Phe	Pro	Asp	Val	Asn	Asp	Val	Asp	Arg	Val	Gly
		115					120					125			
Pro	Thr	Ala	Tyr	Gln	Gly	Arg	Phe	Ala	Val	Pro	Gly	Gly	Tyr	Pro	Ala
	130					135					140				
Tyr	Leu	Lys	Glu	Val	Leu	Asp	Ala	His	Glu	Cys	Ser	Asp	Phe	Phe	Gly
145					150					155				160	
His	Val	Thr	Gln	Arg	Ser	Val	Leu	Val	Glu	Gly	Asp	Val	Arg	Glu	Thr
			165						170					175	
Val	Pro	Arg	Tyr	Leu	Ala	Glu	Asn	Pro	Gln	Thr	Val	Ile	Ala	Leu	Ala
		180						185					190		
Tyr	Phe	Asp	Leu	Asp	Leu	Tyr	Glu	Pro	Thr	Lys	Ala	Val	Leu	Glu	Ala
	195						200					205			
Ile	Arg	Pro	Tyr	Leu	Thr	Lys	Gly	Ser	Ile	Val	Ala	Phe	Asp	Glu	Leu
	210					215						220			
Asp	Asn	Pro	Lys	Trp	Pro	Gly	Glu	Asn	Ile	Ala	Met	Arg	Lys	Val	Leu
225					230					235				240	
Gly	Leu	Asp	His	Ala	Pro	Leu	Arg	Leu	Leu	Pro	Gly	Arg	Pro	Ala	Pro
			245						250					255	
Ala	Tyr	Leu	Arg	Trp	Gly	Asp									
			260												

<210> 13  
 <211> 738  
 <212> DNA  
 <213> Bacteria

<220>

<221> CDS

<222> (1)...(738)

<400> 13

atg	ttc	gga	ccg	gag	cac	gcc	gag	gtg	tac	gag	gcc	gcc	tac	cgc	ggc	48
Met	Phe	Gly	Pro	Glu	His	Ala	Glu	Val	Tyr	Glu	Ala	Ala	Tyr	Arg	Gly	
1				5					10					15		
cgc	ggc	aag	agc	tgg	cac	gac	gag	gcg	gac	gtg	gcc	gac	cgg	atc		96
Arg	Gly	Lys	Ser	Trp	His	Asp	Glu	Ala	Ala	Asp	Val	Ala	Asp	Arg	Ile	

20	25	30	
cgg gcc gcc cgc ccc gac gcc gcc cgg ctg ctc gac gtc ggc tgc ggc			144
Arg Ala Ala Arg Pro Asp Ala Ala Arg Leu Leu Asp Val Gly Cys Gly			
35	40	45	
acc ggc gcg cac ctc gag acc ttc gcg acc cgc ttc ccc cac gtg gag			192
Thr Gly Ala His Leu Glu Thr Phe Ala Thr Arg Phe Pro His Val Glu			
50	55	60	
ggg ctc gaa ctg gcc ccg gcg atg ctg gcg ctc gcc cga cac cgg ctg			240
Gly Leu Glu Leu Ala Pro Ala Met Leu Ala Leu Ala Arg His Arg Leu			
65	70	75	80
ccc ggg gtg cgc ctg cac gcc ggg gac atg cgg acg ttc gac ctt ggc			288
Pro Gly Val Arg Leu His Ala Gly Asp Met Arg Thr Phe Asp Leu Gly			
85	90	95	
gtc acg ttc gac gcg gtg acc tgc ctg ttc acc gcg gtc aac ttc ctc			336
Val Thr Phe Asp Ala Val Thr Cys Leu Phe Thr Ala Val Asn Phe Leu			
100	105	110	
ggc acg gtg gcc gag atg cgg gcg gcc gtg gcc gcg atg tcg gcc cac			384
Gly Thr Val Ala Glu Met Arg Ala Ala Val Ala Ala Met Ser Ala His			
115	120	125	
ctg gcg ccg ggc ggc gtg ctg gtg ctc gaa ccg tgg tgg ttc ccg gag			432
Leu Ala Pro Gly Gly Val Leu Val Leu Glu Pro Trp Trp Phe Pro Glu			
130	135	140	
cgg ttc atc gac ggg tac gtc ggc ggc gac ctg gtg cgc gag gag ggc			480
Arg Phe Ile Asp Gly Tyr Val Gly Gly Asp Leu Val Arg Glu Glu Gly			
145	150	155	160
cgc acg gtg gcg cgg gtg tcg cgg tcc acc cgg cag gga cgg gtg acg			528
Arg Thr Val Ala Arg Val Ser Arg Ser Thr Arg Gln Gly Arg Val Thr			
165	170	175	
cgg atg gag gag cgc tgg ctc gtc ggc gac gcc gcc ggg atc cgg gag			576
Arg Met Glu Glu Arg Trp Leu Val Gly Asp Ala Ala Gly Ile Arg Glu			
180	185	190	
ttc agc cag gtc ggc ctg ctc acc atg ttc acc cgc gag gag tac gac			624
Phe Ser Gln Val Gly Leu Leu Thr Met Phe Thr Arg Glu Glu Tyr Asp			
195	200	205	
gcg gcg ttc gcc gct gcc ggc tgc gag tcc gcg tac gtc gag ggc tgg			672
Ala Ala Phe Ala Ala Ala Gly Cys Glu Ser Ala Tyr Val Glu Gly Trp			
210	215	220	
ctg acc ggc cgg ggc ctt ttc gtg gcg acg cgt acc ggt gga cac gcc			720
Leu Thr Gly Arg Gly Leu Phe Val Ala Thr Arg Thr Gly Gly His Ala			
225	230	235	240
acc ccg aca atg gtt tga			738
Thr Pro Thr Met Val *			
245			



<210> 14  
 <211> 245  
 <212> PRT  
 <213> Bacteria

<400> 14  
 Met Phe Gly Pro Glu His Ala Glu Val Tyr Glu Ala Ala Tyr Arg Gly  
 1 5 10 15  
 Arg Gly Lys Ser Trp His Asp Glu Ala Ala Asp Val Ala Asp Arg Ile  
 20 25 30  
 Arg Ala Ala Arg Pro Asp Ala Ala Arg Leu Leu Asp Val Gly Cys Gly  
 35 40 45  
 Thr Gly Ala His Leu Glu Thr Phe Ala Thr Arg Phe Pro His Val Glu  
 50 55 60  
 Gly Leu Glu Leu Ala Pro Ala Met Leu Ala Leu Arg His Arg Leu  
 65 70 75 80  
 Pro Gly Val Arg Leu His Ala Gly Asp Met Arg Thr Phe Asp Leu Gly  
 85 90 95  
 Val Thr Phe Asp Ala Val Thr Cys Leu Phe Thr Ala Val Asn Phe Leu  
 100 105 110  
 Gly Thr Val Ala Glu Met Arg Ala Ala Val Ala Ala Met Ser Ala His  
 115 120 125  
 Leu Ala Pro Gly Gly Val Leu Val Leu Glu Pro Trp Trp Phe Pro Glu  
 130 135 140  
 Arg Phe Ile Asp Gly Tyr Val Gly Gly Asp Leu Val Arg Glu Glu Gly  
 145 150 155 160  
 Arg Thr Val Ala Arg Val Ser Arg Ser Thr Arg Gln Gly Arg Val Thr  
 165 170 175  
 Arg Met Glu Glu Arg Trp Leu Val Gly Asp Ala Ala Gly Ile Arg Glu  
 180 185 190  
 Phe Ser Gln Val Gly Leu Leu Thr Met Phe Thr Arg Glu Glu Tyr Asp  
 195 200 205  
 Ala Ala Phe Ala Ala Ala Gly Cys Glu Ser Ala Tyr Val Glu Gly Trp  
 210 215 220  
 Leu Thr Gly Arg Gly Leu Phe Val Ala Thr Arg Thr Gly Gly His Ala  
 225 230 235 240  
 Thr Pro Thr Met Val  
 245

<210> 15  
 <211> 1707  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(1707)

<400> 15  
 gtg ccg gac cac gac cag cag cct cgc cac ggc ggc acg ctg cgc tac 48  
 Val Pro Asp His Asp Gln Gln Pro Arg His Gly Gly Thr Leu Arg Tyr  
 1 5 10 15  
 tac ggg ccc ggt ggc ctc gac cac ctg gac ccc gcc gcc gcg tac tac 96  
 Tyr Gly Pro Gly Gly Leu Asp His Leu Asp Pro Ala Ala Ala Tyr Tyr  
 20 25 30

gcc ttc tcc cac cag gtc atc cgg ctc ttc gcc cgg cag ctg ttc agc	144
Ala Phe Ser His Gln Val Ile Arg Leu Phe Ala Arg Gln Leu Phe Ser	
35 40 45	
tac ccg acc acg gag gac gcc gcc gcg ctg gtg ccg gtg ccc gac gtg	192
Tyr Pro Thr Thr Glu Asp Ala Ala Ala Leu Val Pro Val Pro Asp Val	
50 55 60	
gcc gcc gag ttg ccc acg gtg gac aat ggc ggg ctc agc gag gac ggc	240
Ala Ala Glu Leu Pro Thr Val Asp Asn Gly Gly Leu Ser Glu Asp Gly	
65 70 75 80	
cgc acg tac acg atc cgc ctg cgc gac ggg gtc cgg tgg gac acc gcc	288
Arg Thr Tyr Thr Ile Arg Leu Arg Asp Gly Val Arg Trp Asp Thr Ala	
85 90 95	
ccg ccg cgg ccg gtg acc gcg ggg gac ttc gtg cgc ggc ttc aag cgg	336
Pro Pro Arg Pro Val Thr Ala Gly Asp Phe Val Arg Gly Phe Lys Arg	
100 105 110	
atg gcc aac ccg gtc gcc ggg gcc ggc gcc atc gcc tac tac acg agc	384
Met Ala Asn Pro Val Ala Gly Ala Gly Ala Ile Ala Tyr Tyr Thr Ser	
115 120 125	
acc atc gcc ggc atg gcg gag ttc gcc gag ggc tac cgc gcg cgc ttc	432
Thr Ile Ala Gly Met Ala Glu Phe Ala Glu Gly Tyr Arg Ala Arg Phe	
130 135 140	
gcc ggg cgt acg ccc acc gcc gcc gag ctg gcc gac tac cag aac ggc	480
Ala Gly Arg Thr Pro Thr Ala Ala Glu Leu Ala Asp Tyr Gln Asn Gly	
145 150 155 160	
cac gag atc agc ggg ctg tgg gcc aag gac gac cgg acc ctg gtg atc	528
His Glu Ile Ser Gly Leu Trp Ala Lys Asp Asp Arg Thr Leu Val Ile	
165 170 175	
gag ctg ctg cgc ccc gcc aac gac atg ctc aac ctg ctg gcg atg ccg	576
Glu Leu Leu Arg Pro Ala Asn Asp Met Leu Asn Leu Leu Ala Met Pro	
180 185 190	
ttc gcc tcc gcc gcg ccc cgg gag ttc gac gac ctc gtc ccg gac ggt	624
Phe Ala Ser Ala Ala Pro Arg Glu Phe Asp Asp Leu Val Pro Asp Gly	
195 200 205	
ccg gac ttc gcg cgg ctg gtc cgc tcc aac ggg ccg tac cgg atc acc	672
Pro Asp Phe Ala Arg Leu Val Arg Ser Asn Gly Pro Tyr Arg Ile Thr	
210 215 220	
ggc tac gcc cgg ggc agc cac ctg acc atg gac cac aac ccc gcc tgg	720
Gly Tyr Ala Arg Gly Ser His Leu Thr Met Asp His Asn Pro Ala Trp	
225 230 235 240	
cgg gcc gac gca gac ccg atc cgc cgc cgc tac gtg gac cgt atc gag	768
Arg Ala Asp Ala Asp Pro Ile Arg Arg Arg Tyr Val Asp Arg Ile Glu	
245 250 255	
gtg cgg atg gcg agg gtg agc gac gag cgg gtc cgc gcc gag atc gag	816
Val Arg Met Ala Arg Val Ser Asp Glu Arg Val Arg Ala Glu Ile Glu	



atc gac cgc gcg ttg tcc gcc cgg acg gag gcc gag gcg gag gag ctg 1536  
 Ile Asp Arg Ala Leu Ser Ala Arg Thr Glu Ala Glu Ala Glu Glu Leu  
 500 505 510  
  
 tgg cac cgg gtc gac cgg cag gtg ctg cag gac gtg gcg atc gtg ccg 1584  
 Trp His Arg Val Asp Arg Gln Val Leu Gln Asp Val Ala Ile Val Pro  
 515 520 525  
  
 atc ctg gcc tgc gag ccg acc atc gag cac ctg acc agt tcc cgg gtg 1632  
 Ile Leu Ala Cys Glu Pro Thr Ile Glu His Leu Thr Ser Ser Arg Val  
 530 535 540  
  
 cgg ggg gcg atc ccg ctg ccg cac gtg gac cgc tgg tac gac gcg gcg 1680  
 Arg Gly Ala Ile Pro Leu Pro His Val Asp Arg Trp Tyr Asp Ala Ala  
 545 550 555 560  
  
 aac ctc tgg ctg gac ccg ccc gac tga 1707  
 Asn Leu Trp Leu Asp Pro Pro Asp \*  
 565

<210> 16  
 <211> 568  
 <212> PRT  
 <213> Bacteria

<400> 16  
 Val Pro Asp His Asp Gln Gln Pro Arg His Gly Gly Thr Leu Arg Tyr  
 1 5 10 15  
 Tyr Gly Pro Gly Gly Leu Asp His Leu Asp Pro Ala Ala Ala Tyr Tyr  
 20 25 30  
 Ala Phe Ser His Gln Val Ile Arg Leu Phe Ala Arg Gln Leu Phe Ser  
 35 40 45  
 Tyr Pro Thr Thr Glu Asp Ala Ala Leu Val Pro Val Pro Asp Val  
 50 55 60  
 Ala Ala Glu Leu Pro Thr Val Asp Asn Gly Gly Leu Ser Glu Asp Gly  
 65 70 75 80  
 Arg Thr Tyr Thr Ile Arg Leu Arg Asp Gly Val Arg Trp Asp Thr Ala  
 85 90 95  
 Pro Pro Arg Pro Val Thr Ala Gly Asp Phe Val Arg Gly Phe Lys Arg  
 100 105 110  
 Met Ala Asn Pro Val Ala Gly Ala Gly Ala Ile Ala Tyr Tyr Thr Ser  
 115 120 125  
 Thr Ile Ala Gly Met Ala Glu Phe Ala Glu Gly Tyr Arg Ala Arg Phe  
 130 135 140  
 Ala Gly Arg Thr Pro Thr Ala Ala Glu Leu Ala Asp Tyr Gln Asn Gly  
 145 150 155 160  
 His Glu Ile Ser Gly Leu Trp Ala Lys Asp Asp Arg Thr Leu Val Ile  
 165 170 175  
 Glu Leu Leu Arg Pro Ala Asn Asp Met Leu Asn Leu Leu Ala Met Pro  
 180 185 190  
 Phe Ala Ser Ala Ala Pro Arg Glu Phe Asp Asp Leu Val Pro Asp Gly  
 195 200 205  
 Pro Asp Phe Ala Arg Leu Val Arg Ser Asn Gly Pro Tyr Arg Ile Thr  
 210 215 220  
 Gly Tyr Ala Arg Gly Ser His Leu Thr Met Asp His Asn Pro Ala Trp  
 225 230 235 240  
 Arg Ala Asp Ala Asp Pro Ile Arg Arg Arg Tyr Val Asp Arg Ile Glu

245 250 255  
 Val Arg Met Ala Arg Val Ser Asp Glu Arg Val Arg Ala Glu Ile Glu  
 260 265 270  
 Ser Gly Ala Ala Asp Leu Ser Trp Gly Ala Ala Val Gly Arg Pro Arg  
 275 280 285  
 Arg Arg Thr Ala Ala Asp Arg Asn Leu Gly Trp Ala Leu Asn Pro Tyr  
 290 295 300  
 Leu Ala Phe Asn Leu His Ser Pro His Glu Arg Gly Ala Leu Arg Asp  
 305 310 315 320  
 Arg Thr Val Arg Leu Ala Ile Ala Tyr Ala Val Asp Lys Ala Arg Leu  
 325 330 335  
 Val Arg Phe Phe Asp Asp Met Asn Ile Gly Thr Val Thr Arg Pro Ala  
 340 345 350  
 His Thr Ala Ile Pro Pro Gly Asn Phe Gly His Arg Glu Tyr Asp Pro  
 355 360 365  
 Tyr Pro Thr Pro Gly Asp Arg Gly Asp Arg Ala Arg Cys Arg Glu Leu  
 370 375 380  
 Leu Ala Glu Ala Gly Tyr Pro Asp Gly Leu Arg Leu Thr Met Ile Tyr  
 385 390 395 400  
 Arg Ile Asp Ala Val His Gly Gln Val Ala Lys Ala Ile Ala Glu Asp  
 405 410 415  
 Leu Gly Ala Gly Gly Val Asp Val Arg Leu Val Glu Ile Asp Gln Thr  
 420 425 430  
 Asp Glu Tyr Tyr Arg Ile Leu Gln Asp Pro Ala Arg Ala Ala Ala Gly  
 435 440 445  
 Glu Trp Asp Ile Thr Pro Ala Ala Trp Met Pro Asp Trp Phe Gly Asn  
 450 455 460  
 Asn Gly Arg Ser Tyr Val Gln Pro Met Phe Gln Ser Asn Thr Gly Val  
 465 470 475 480  
 Gly Thr Ala Asn Tyr Gly Gly Tyr His Asn Pro Leu Val Asp Glu Leu  
 485 490 495  
 Ile Asp Arg Ala Leu Ser Ala Arg Thr Glu Ala Glu Ala Glu Glu Leu  
 500 505 510  
 Trp His Arg Val Asp Arg Gln Val Leu Gln Asp Val Ala Ile Val Pro  
 515 520 525  
 Ile Leu Ala Cys Glu Pro Thr Ile Glu His Leu Thr Ser Ser Arg Val  
 530 535 540  
 Arg Gly Ala Ile Pro Leu Pro His Val Asp Arg Trp Tyr Asp Ala Ala  
 545 550 555 560  
 Asn Leu Trp Leu Asp Pro Pro Asp  
 565

<210> 17  
 <211> 999  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(999)

<400> 17  
 atg gac agg ttg cag tcg gcg ctg gcc ctc tac gag gag gcg atg ggc 48  
 Met Asp Arg Leu Gln Ser Ala Leu Ala Leu Tyr Glu Glu Ala Met Gly  
 1 5 10 15  
 tac acg tac gcg gca gcc ctg cgg gcc gcc gcc gcc gtc ggc gtc gcc 96

Tyr	Thr	Tyr	Ala	Ala	Ala	Leu	Arg	Ala	Ala	Ala	Ala	Val	Gly	Val	Ala	
			20					25					30			
gac	cac	ctg	gtc	gac	ggc	ccc	cgt	acg	ccc	gcc	gag	ctg	gcc	gcc	gcg	144
Asp	His	Leu	Val	Asp	Gly	Pro	Arg	Thr	Pro	Ala	Glu	Leu	Ala	Ala	Ala	
		35					40					45				
acg	ggc	acc	gac	gcg	gac	gcg	ctc	cgc	cgg	gtg	ctg	cgc	ctg	ctg	gcg	192
Thr	Gly	Thr	Asp	Ala	Asp	Ala	Leu	Arg	Arg	Val	Leu	Arg	Leu	Leu	Ala	
	50					55					60					
gtc	cgc	gac	gtg	gtc	cgc	gag	tcc	gac	ggc	cgg	ttc	gcg	ctg	acc	gac	240
Val	Arg	Asp	Val	Val	Arg	Glu	Ser	Asp	Gly	Arg	Phe	Ala	Leu	Thr	Asp	
	65				70				75					80		
aag	ggc	gcg	gcg	ctg	cgg	tcg	gac	tcg	cgc	gtg	ccc	gcg	cgg	gcc	ggc	288
Lys	Gly	Ala	Ala	Leu	Arg	Ser	Asp	Ser	Pro	Val	Pro	Ala	Arg	Ala	Gly	
			85						90				95			
atc	ctc	atg	ttc	acc	gac	acg	atg	ttc	tgg	acg	atg	agt	cac	cgg	gtg	336
Ile	Leu	Met	Phe	Thr	Asp	Thr	Met	Phe	Trp	Thr	Met	Ser	His	Arg	Val	
			100					105					110			
gcg	agc	gcg	ctg	ggg	cgc	gag	cga	ccc	gcc	ttc	gcc	gac	atc	ttc	ggt	384
Ala	Ser	Ala	Leu	Gly	Pro	Glu	Arg	Pro	Ala	Phe	Ala	Asp	Ile	Phe	Gly	
		115					120					125				
agc	tcg	ctg	gac	gcc	tac	ttc	gac	ggc	gac	gcc	gag	gtc	gag	gcg	ctc	432
Ser	Ser	Leu	Asp	Ala	Tyr	Phe	Asp	Gly	Asp	Ala	Glu	Val	Glu	Ala	Leu	
	130					135					140					
tac	tac	gag	ggc	atg	gaa	acg	gtc	agc	gcg	gcg	gag	cac	ctc	att	ctc	480
Tyr	Tyr	Glu	Gly	Met	Glu	Thr	Val	Ser	Ala	Ala	Glu	His	Leu	Ile	Leu	
	145				150				155					160		
gcc	cgc	gcc	ggt	gac	ttc	ccc	gcc	acc	ggc	acc	gtg	gcg	gac	gtc	ggc	528
Ala	Arg	Ala	Gly	Asp	Phe	Pro	Ala	Thr	Gly	Thr	Val	Ala	Asp	Val	Gly	
			165						170					175		
ggc	ggc	cgg	ggc	ggc	ttc	ctg	ctc	acc	gtc	cta	cgc	gag	cac	ccc	ggc	576
Gly	Gly	Arg	Gly	Gly	Phe	Leu	Leu	Thr	Val	Leu	Arg	Glu	His	Pro	Gly	
			180					185					190			
ctg	cag	ggc	gtg	ctg	ctg	gac	cgc	gcg	gag	gtg	gtc	gcc	cgg	cac	cgg	624
Leu	Gln	Gly	Val	Leu	Leu	Asp	Arg	Ala	Glu	Val	Val	Ala	Arg	His	Arg	
		195					200					205				
ctg	gac	gcc	ccg	gac	gtg	gcg	ggg	cgc	tgg	aag	gtt	gtc	gag	ggc	gac	672
Leu	Asp	Ala	Pro	Asp	Val	Ala	Gly	Arg	Trp	Lys	Val	Val	Glu	Gly	Asp	
	210					215					220					
ttc	ctc	cgc	gag	gtg	ccc	cac	gcc	gac	gtg	cac	gtg	ctc	aag	cgc	atc	720
Phe	Leu	Arg	Glu	Val	Pro	His	Ala	Asp	Val	His	Val	Leu	Lys	Arg	Ile	
	225				230				235						240	
ctg	cac	aac	tgg	ggc	gac	gag	gac	agc	gtc	cgg	atc	ctg	acg	aac	tgc	768
Leu	His	Asn	Trp	Gly	Asp	Glu	Asp	Ser	Val	Arg	Ile	Leu	Thr	Asn	Cys	
			245					250						255		

cgc cgg gtc atg ccc gcg cac ggc cgg gtg ctc gtg atc gac gcg gtc	816
Arg Arg Val Met Pro Ala His Gly Arg Val Leu Val Ile Asp Ala Val	
260 265 270	
gtc ccc gag ggc aac gac gcg cac cag agc aag gag atg gac ttc atg	864
Val Pro Glu Gly Asn Asp Ala His Gln Ser Lys Glu Met Asp Phe Met	
275 280 285	
atg ctc gcc gcg cgc acc ggc cag gaa cgc acc gcc gcc gag ctg gag	912
Met Leu Ala Ala Arg Thr Gly Gln Glu Arg Thr Ala Ala Glu Leu Glu	
290 295 300	
ccg ttg ttc acc gcg gcc ggg ctg cgc ctg gac cgg gtc gtc ggc acc	960
Pro Leu Phe Thr Ala Ala Gly Leu Arg Leu Asp Arg Val Val Gly Thr	
305 310 315 320	
tcg tcg gtc atg tcc atc gcg gtc ggc gtg ccg gcc tga	999
Ser Ser Val Met Ser Ile Ala Val Gly Val Pro Ala *	
325 330	

<210> 18  
 <211> 332  
 <212> PRT  
 <213> Bacteria

<400> 18

Met Asp Arg Leu Gln Ser Ala Leu Ala Leu Tyr Glu Glu Ala Met Gly	
1 5 10 15	
Tyr Thr Tyr Ala Ala Leu Arg Ala Ala Ala Val Gly Val Ala	
20 25 30	
Asp His Leu Val Asp Gly Pro Arg Thr Pro Ala Glu Leu Ala Ala	
35 40 45	
Thr Gly Thr Asp Ala Asp Ala Leu Arg Arg Val Leu Arg Leu Leu Ala	
50 55 60	
Val Arg Asp Val Val Arg Glu Ser Asp Gly Arg Phe Ala Leu Thr Asp	
65 70 75 80	
Lys Gly Ala Ala Leu Arg Ser Asp Ser Pro Val Pro Ala Arg Ala Gly	
85 90 95	
Ile Leu Met Phe Thr Asp Thr Met Phe Trp Thr Met Ser His Arg Val	
100 105 110	
Ala Ser Ala Leu Gly Pro Glu Arg Pro Ala Phe Ala Asp Ile Phe Gly	
115 120 125	
Ser Ser Leu Asp Ala Tyr Phe Asp Gly Asp Ala Glu Val Glu Ala Leu	
130 135 140	
Tyr Tyr Glu Gly Met Glu Thr Val Ser Ala Ala Glu His Leu Ile Leu	
145 150 155 160	
Ala Arg Ala Gly Asp Phe Pro Ala Thr Gly Thr Val Ala Asp Val Gly	
165 170 175	
Gly Gly Arg Gly Gly Phe Leu Leu Thr Val Leu Arg Glu His Pro Gly	
180 185 190	
Leu Gln Gly Val Leu Leu Asp Arg Ala Glu Val Val Ala Arg His Arg	
195 200 205	
Leu Asp Ala Pro Asp Val Ala Gly Arg Trp Lys Val Val Glu Gly Asp	
210 215 220	
Phe Leu Arg Glu Val Pro His Ala Asp Val His Val Leu Lys Arg Ile	
225 230 235 240	

Leu His Asn Trp Gly Asp Glu Asp Ser Val Arg Ile Leu Thr Asn Cys  
                                   245                                  250                                  255  
 Arg Arg Val Met Pro Ala His Gly Arg Val Leu Val Ile Asp Ala Val  
                                   260                                  265                                  270  
 Val Pro Glu Gly Asn Asp Ala His Gln Ser Lys Glu Met Asp Phe Met  
                                   275                                  280                                  285  
 Met Leu Ala Ala Arg Thr Gly Gln Glu Arg Thr Ala Ala Glu Leu Glu  
                                   290                                  295                                  300  
 Pro Leu Phe Thr Ala Ala Gly Leu Arg Leu Asp Arg Val Val Gly Thr  
 305                                  310                                  315                                  320  
 Ser Ser Val Met Ser Ile Ala Val Gly Val Pro Ala  
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 ccg gcg cag agt ccg ctg cgc acc gcg tcc tgg gcc cgc atc cgc gag 96  
 Pro Ala Gln Ser Pro Leu Arg Thr Ala Ser Trp Ala Arg Ile Arg Glu  
                                   20                                  25                                  30  
  
 ctg ttc gcc ctg gac ccg acg acc gtg cac ctc aac acg ggg acg gtc 144  
 Leu Phe Ala Leu Asp Pro Thr Thr Val His Leu Asn Thr Gly Thr Val  
                                   35                                  40                                  45  
  
 ggc gcc atg ccg tac gag gtg ctg gac acc gtg gac cgg gtg acc cgc 192  
 Gly Ala Met Pro Tyr Glu Val Leu Asp Thr Val Asp Arg Val Thr Arg  
                                   50                                  55                                  60  
  
 cag tgg acc ggc ggc ctg ctc gac gtc tac cgc ccg gcg atg ttc acc 240  
 Gln Trp Thr Gly Gly Leu Leu Asp Val Tyr Arg Pro Ala Met Phe Thr  
   65                                  70                                  75                                  80  
  
 gag tac cgg gac gcc atc gcg aag acg ttc ggc gtg gac ggc gac gag 288  
 Glu Tyr Arg Asp Ala Ile Ala Lys Thr Phe Gly Val Asp Gly Asp Glu  
                                   85                                  90                                  95  
  
 atc gtg atc tgc cac aac gcc acc gag ggg gtc gcc cgg gtc atc cac 336  
 Ile Val Ile Cys His Asn Ala Thr Glu Gly Val Ala Arg Val Ile His  
                                   100                                  105                                  110  
  
 ggc ctc gac ctg cgc gag ggc gac gag gtg gtg acg acc acg cac gag 384  
 Gly Leu Asp Leu Arg Glu Gly Asp Glu Val Val Thr Thr Thr His Glu  
                                   115                                  120                                  125  
  
 tgc tac tcc gtg ctg tcc aac ttc aac ctg ctg cgc aac cgg ttc ggg 432  
 Cys Tyr Ser Val Leu Ser Asn Phe Asn Leu Leu Arg Asn Arg Phe Gly



130	135	140	
gtg gtg ctg aag acc gtc acc ccg ccg tcc ggc cac gag gtg cgc gcg			480
Val Val Leu Lys Thr Val Thr Pro Pro Ser Gly His Glu Val Arg Ala			
145	150	155	160
gag gag atc gtc gag ctg gtc gag gcc gcc atc acg ccc cgg acg aag			528
Glu Glu Ile Val Glu Leu Val Glu Ala Ala Ile Thr Pro Arg Thr Lys			
	165	170	175
gtg ctc tcg ttc gcc gcg atc acc ctc ttc acc ggg acg atg ttc ccc			576
Val Leu Ser Phe Ala Ala Ile Thr Leu Phe Thr Gly Thr Met Phe Pro			
	180	185	190
atc cgg cag ctc tgc gag ctg gcg cac cgg cac ggg ctg acc acc gtc			624
Ile Arg Gln Leu Cys Glu Leu Ala His Arg His Gly Leu Thr Thr Val			
	195	200	205
atc gac ggc gcg ctg atc ccc ggc atg ctc gac tgc gac ctg cgc gcg			672
Ile Asp Gly Ala Leu Ile Pro Gly Met Leu Asp Cys Asp Leu Arg Ala			
	210	215	220
acc ggg gcg gac ttc atc acc tgc tcc ggg tcg aag ttc cag tgc ggc			720
Thr Gly Ala Asp Phe Ile Thr Cys Ser Gly Ser Lys Phe Gln Cys Gly			
	225	230	235
ccg ctc ggc acc ggc ctg atc tac gtc cgc aac aag gtc gtc ccc gag			768
Pro Leu Gly Thr Gly Leu Ile Tyr Val Arg Asn Lys Val Val Pro Glu			
	245	250	255
cac aac ccc ctg ccg ctg ccc acg ttc tgg ccg ctc atc tcg acc tgg			816
His Asn Pro Leu Pro Leu Pro Thr Phe Trp Pro Leu Ile Ser Thr Trp			
	260	265	270
tac ccg atg atg ggc agc ccg ccg ccg cgg acc agc acc gcc gtg gag			864
Tyr Pro Met Met Gly Ser Pro Pro Pro Arg Thr Ser Thr Ala Val Glu			
	275	280	285
agc tac aac atg ggc gac ttc ctg cag agc gcc ggc agc gcc aac ctg			912
Ser Tyr Asn Met Gly Asp Phe Leu Gln Ser Ala Gly Ser Ala Asn Leu			
	290	295	300
gcg cgg ggc gcc gcc ctg gcc cgg gcc ttc gag ctg tgg gac gac atc			960
Ala Arg Gly Ala Ala Leu Ala Arg Ala Phe Glu Leu Trp Asp Asp Ile			
	305	310	315
ggc cgc gac cgc atc gag gcg tac atc atg gac ctc gcc gag tac gcc			1008
Gly Arg Asp Arg Ile Glu Ala Tyr Ile Met Asp Leu Ala Glu Tyr Ala			
	325	330	335
cgc ggc cgg ctc atc gac gcg ttc ggc gtc gag gcc atg tac tcc ccc			1056
Arg Gly Arg Leu Ile Asp Ala Phe Gly Val Glu Ala Met Tyr Ser Pro			
	340	345	350
ggc gcc gac ccg cgg ctg cgc tcg ccg ctg ctc gcg ttc aac ccg ttc			1104
Gly Ala Asp Pro Arg Leu Arg Ser Pro Leu Leu Ala Phe Asn Pro Phe			
	355	360	365

cgg	cgg	ccg	gag	gac	gcc	tgg	aac	atc	aag	aag	ttc	atc	ggc	ttc	gtc	1152
Arg	Arg	Pro	Glu	Asp	Ala	Trp	Asn	Ile	Lys	Lys	Phe	Ile	Gly	Phe	Val	
370						375					380					
aag	cgc	ctg	gag	acc	gag	cac	cgg	atc	tgg	acc	cgc	tgg	acg	gag	ttc	1200
Lys	Arg	Leu	Glu	Thr	Glu	His	Arg	Ile	Trp	Thr	Arg	Trp	Thr	Glu	Phe	
385					390					395					400	
gac	gtg	ccc	ggc	tcc	ccg	cac	cag	cac	tac	gcg	gcg	cgc	atc	acc	acg	1248
Asp	Val	Pro	Gly	Ser	Pro	His	Gln	His	Tyr	Ala	Ala	Arg	Ile	Thr	Thr	
				405					410					415		
cac	ctg	ttc	aac	acc	cgg	gaa	gag	atc	gac	cac	acc	gta	cgg	acg	atg	1296
His	Leu	Phe	Asn	Thr	Arg	Glu	Glu	Ile	Asp	His	Thr	Val	Arg	Thr	Met	
			420					425					430			
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Val	Arg	Leu	Ala	Glu	Glu	Met	Ser	*								
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Leu	Phe	Ala	Leu	Asp	Pro	Thr	Thr	Val	His	Leu	Asn	Thr	Gly	Thr	Val	
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Gly	Ala	Met	Pro	Tyr	Glu	Val	Leu	Asp	Thr	Val	Asp	Arg	Val	Thr	Arg	
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Gln	Trp	Thr	Gly	Gly	Leu	Leu	Asp	Val	Tyr	Arg	Pro	Ala	Met	Phe	Thr	
65				70					75						80	
Glu	Tyr	Arg	Asp	Ala	Ile	Ala	Lys	Thr	Phe	Gly	Val	Asp	Gly	Asp	Glu	
			85					90					95			
Ile	Val	Ile	Cys	His	Asn	Ala	Thr	Glu	Gly	Val	Ala	Arg	Val	Ile	His	
			100					105					110			
Gly	Leu	Asp	Leu	Arg	Glu	Gly	Asp	Glu	Val	Val	Thr	Thr	Thr	His	Glu	
	115						120					125				
Cys	Tyr	Ser	Val	Leu	Ser	Asn	Phe	Asn	Leu	Leu	Arg	Asn	Arg	Phe	Gly	
130						135					140					
Val	Val	Leu	Lys	Thr	Val	Thr	Pro	Pro	Ser	Gly	His	Glu	Val	Arg	Ala	
145					150					155					160	
Glu	Glu	Ile	Val	Glu	Leu	Val	Glu	Ala	Ala	Ile	Thr	Pro	Arg	Thr	Lys	
			165					170						175		
Val	Leu	Ser	Phe	Ala	Ala	Ile	Thr	Leu	Phe	Thr	Gly	Thr	Met	Phe	Pro	
			180					185					190			
Ile	Arg	Gln	Leu	Cys	Glu	Leu	Ala	His	Arg	His	Gly	Leu	Thr	Thr	Val	
	195						200					205				
Ile	Asp	Gly	Ala	Leu	Ile	Pro	Gly	Met	Leu	Asp	Cys	Asp	Leu	Arg	Ala	
210						215					220					
Thr	Gly	Ala	Asp	Phe	Ile	Thr	Cys	Ser	Gly	Ser	Lys	Phe	Gln	Cys	Gly	
225					230						235				240	
Pro	Leu	Gly	Thr	Gly	Leu	Ile	Tyr	Val	Arg	Asn	Lys	Val	Val	Pro	Glu	



Asn	Ala	Gly	Leu	Gly	Ala	Ser	His	Arg	Ser	Tyr	Val	Val	His	Leu	Arg		
				85					90					95			
ccc	ggg	gtg	ctc	tgg	gac	acg	ccg	acc	ccc	cgc	ccg	gtg	acg	gcg	cac	336	
Pro	Gly	Val	Leu	Trp	Asp	Thr	Pro	Thr	Pro	Arg	Pro	Val	Thr	Ala	His		
			100					105					110				
gac	gtc	gta	cgc	ggc	ttc	aag	cgg	ctg	gcc	aac	ccg	ctc	acc	cga	cac	384	
Asp	Val	Val	Arg	Gly	Phe	Lys	Arg	Leu	Ala	Asn	Pro	Leu	Thr	Arg	His		
			115				120					125					
ccc	gcg	ctg	gcg	tac	ttc	cgg	ggc	acc	ctg	cgg	ggc	atg	ggc	cgg	tac	432	
Pro	Ala	Leu	Ala	Tyr	Phe	Arg	Gly	Thr	Leu	Arg	Gly	Met	Gly	Arg	Tyr		
	130					135					140						
tgc	gac	gag	tac	gcg	gcg	gcg	gtc	gcc	ggc	cac	ccg	gtc	acc	gcg	gcg	480	
Cys	Asp	Glu	Tyr	Ala	Ala	Ala	Val	Ala	Gly	His	Pro	Val	Thr	Ala	Ala		
145					150					155					160		
ctg	ctc	gcc	ggc	ttc	cag	gac	gcc	cac	gag	atc	ccc	ggc	gtg	ttc	gcc	528	
Leu	Leu	Ala	Gly	Phe	Gln	Asp	Ala	His	Glu	Ile	Pro	Gly	Val	Phe	Ala		
				165					170					175			
gtc	gac	gac	gag	acg	gtg	gtc	ttc	gag	ctg	gac	cgt	ccg	gcg	ctg	gac	576	
Val	Asp	Asp	Glu	Thr	Val	Val	Phe	Glu	Leu	Asp	Arg	Pro	Ala	Leu	Asp		
			180					185					190				
ttc	gtc	gac	atg	ctg	gcg	cag	agc	ggc	gcc	tcc	ccg	gcc	ccg	gtg	gag	624	
Phe	Val	Asp	Met	Leu	Ala	Gln	Ser	Gly	Ala	Ser	Pro	Ala	Pro	Val	Glu		
			195				200					205					
tac	gac	gca	cac	ctg	ccg	gga	agc	gcc	ggc	ctg	cac	gag	cac	ctg	gtc	672	
Tyr	Asp	Ala	His	Leu	Pro	Gly	Ser	Ala	Gly	Leu	His	Glu	His	Leu	Val		
	210					215					220						
gcc	aac	ggc	ccg	tac	cgc	gtc	gtg	tgc	tgg	cgc	ccc	ggg	ggc	acc	atc	720	
Ala	Asn	Gly	Pro	Tyr	Arg	Val	Val	Ser	Trp	Arg	Pro	Gly	Gly	Thr	Ile		
225					230					235					240		
cgg	ctg	gag	ccg	aac	ccg	gcg	tgg	cgg	gcg	gag	acc	gac	ccg	atc	cgc	768	
Arg	Leu	Glu	Pro	Asn	Pro	Ala	Trp	Arg	Ala	Glu	Thr	Asp	Pro	Ile	Arg		
				245					250					255			
gag	cgg	cgg	ttc	gac	gcc	gtc	gag	ttc	cgc	gtc	gcc	atg	ggc	ggg	ccg	816	
Glu	Arg	Arg	Phe	Asp	Ala	Val	Glu	Phe	Arg	Val	Ala	Met	Gly	Gly	Pro		
			260					265					270				
cgc	gaa	ctg	gcc	gac	cgg	ctc	gcc	gcc	gac	gac	gcc	gac	ctg	ccg	tgg	864	
Arg	Glu	Leu	Ala	Asp	Arg	Leu	Ala	Ala	Asp	Asp	Ala	Asp	Leu	Pro	Trp		
			275				280					285					
ggc	gtg	ccg	atc	ggc	ccg	gtg	ccc	ggt	cag	cgg	ctc	gac	ccg	tgc	ctg	912	
Gly	Val	Pro	Ile	Gly	Pro	Val	Pro	Gly	Gln	Arg	Leu	Asp	Pro	Cys	Leu		
	290					295					300						
gtg	ttc	aac	ctg	cgc	gac	ccc	gcc	aac	ccg	gcc	gtc	gcc	gac	gcc	gcg	960	
Val	Phe	Asn	Leu	Arg	Asp	Pro	Ala	Asn	Pro	Ala	Val	Ala	Asp	Ala	Ala		
305					310					315					320		

gtg cgc cgg gtc gtc gcc ggg gcg gtc gac cgg gcg gcg ctg gtg cgc	1008
Val Arg Arg Val Val Ala Gly Ala Val Asp Arg Ala Ala Leu Val Arg	
325 330 335	
atc gcc cgg gcc gcc gac ccg tgg tcc gag gtc cgc gcc gcg cac acc	1056
Ile Ala Arg Ala Ala Asp Pro Trp Ser Glu Val Arg Ala Ala His Thr	
340 345 350	
gtc gtg ccg ccc ggc aac gac ggg cac cgg cag ccc gac ccg ctc acc	1104
Val Val Pro Pro Gly Asn Asp Gly His Arg Gln Pro Asp Pro Leu Thr	
355 360 365	
gac ccg att ccc gac gcc gac gcg gac ccg cgc gag cgg ctc gcc gcc	1152
Asp Pro Ile Pro Asp Ala Asp Ala Asp Pro Arg Glu Arg Leu Ala Ala	
370 375 380	
gcg ggg cac ccg gac ggg ctc acc ctg acc gcg gtg cac ccc gac acg	1200
Ala Gly His Pro Asp Gly Leu Thr Leu Thr Ala Val His Pro Asp Thr	
385 390 395 400	
gcc gag gac ctg gcg ctg gcc cgc tgc tgg gcg gcc gac ctc ggc gcc	1248
Ala Glu Asp Leu Ala Leu Ala Arg Ser Trp Ala Ala Asp Leu Gly Ala	
405 410 415	
gcc ggc atc gac gta cgc ctg gtc gcg ctc gac gac gcc aac cac cgg	1296
Ala Gly Ile Asp Val Arg Leu Val Ala Leu Asp Asp Ala Asn His Arg	
420 425 430	
gcc ctg ctc gcc gcc acg ggc gac gcg ccc ggc ctg cga tgg gac ctg	1344
Ala Leu Leu Ala Ala Thr Gly Asp Ala Pro Gly Leu Arg Trp Asp Leu	
435 440 445	
gcg acc gcc acg ttc acc gcg ccg tgg gcc tac ggc aac gcc cgg gtg	1392
Ala Thr Ala Thr Phe Thr Ala Pro Trp Ala Tyr Gly Asn Ala Arg Val	
450 455 460	
ttc ctg caa ccg ctg gtc ggc gag gga ccc ggc aac ccc ggc ggc tac	1440
Phe Leu Gln Pro Leu Val Gly Glu Gly Pro Gly Asn Pro Gly Gly Tyr	
465 470 475 480	
cgc gac ccc ggg gtt gac cgg gtg gtc gag cgc gcg ctg gac gcg gcc	1488
Arg Asp Pro Gly Val Asp Arg Val Val Glu Arg Ala Leu Asp Ala Ala	
485 490 495	
gac ccg cgc gag gcg gtc gcc ctg tgg cag gag gtg gag cgg cgg ctg	1536
Asp Pro Arg Glu Ala Val Ala Leu Trp Gln Glu Val Glu Arg Arg Leu	
500 505 510	
ctc gcc gac gcc gcg gtc gta ccc ctg ctg ttc cgg cgg gcc acg gac	1584
Leu Ala Asp Ala Ala Val Val Pro Leu Leu Phe Arg Arg Ala Thr Asp	
515 520 525	
gcc gcg ccg cgc ggg ccc cgg gtg cgg cgc gcg acc gcc ctg ccg gcg	1632
Ala Ala Pro Arg Gly Pro Arg Val Arg Arg Ala Thr Ala Leu Pro Ala	
530 535 540	
ctc gcc ggc ctg ccc gac ctc gcc gac gtg cgg ctc ggg gtg gac cgg	1680

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tga  
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1683

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Ala	Ala	Ala	Trp	Ser	Pro	Ala	Glu	Arg	Gln	Leu	Leu	Arg	Leu	Cys	Thr
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Arg	Gln	Leu	Ile	Ser	Tyr	Arg	Pro	Glu	Pro	Asp	Pro	Gly	Asp	Trp	Arg
	50				55					60					
Ala	Leu	Ala	Pro	Val	Ala	Asp	Leu	Ala	Thr	Asp	Val	Pro	Ser	Thr	Tyr
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Asn	Ala	Gly	Leu	Gly	Ala	Ser	His	Arg	Ser	Tyr	Val	Val	His	Leu	Arg
		85						90					95		
Pro	Gly	Val	Leu	Trp	Asp	Thr	Pro	Thr	Pro	Arg	Pro	Val	Thr	Ala	His
	100					105						110			
Asp	Val	Val	Arg	Gly	Phe	Lys	Arg	Leu	Ala	Asn	Pro	Leu	Thr	Arg	His
	115				120						125				
Pro	Ala	Leu	Ala	Tyr	Phe	Arg	Gly	Thr	Leu	Arg	Gly	Met	Gly	Arg	Tyr
	130				135						140				
Cys	Asp	Glu	Tyr	Ala	Ala	Val	Ala	Gly	His	Pro	Val	Thr	Ala	Ala	
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Leu	Leu	Ala	Gly	Phe	Gln	Asp	Ala	His	Glu	Ile	Pro	Gly	Val	Phe	Ala
		165						170					175		
Val	Asp	Asp	Glu	Thr	Val	Val	Phe	Glu	Leu	Asp	Arg	Pro	Ala	Leu	Asp
	180						185					190			
Phe	Val	Asp	Met	Leu	Ala	Gln	Ser	Gly	Ala	Ser	Pro	Ala	Pro	Val	Glu
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Tyr	Asp	Ala	His	Leu	Pro	Gly	Ser	Ala	Gly	Leu	His	Glu	His	Leu	Val
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Ala	Asn	Gly	Pro	Tyr	Arg	Val	Val	Ser	Trp	Arg	Pro	Gly	Gly	Thr	Ile
225				230					235					240	
Arg	Leu	Glu	Pro	Asn	Pro	Ala	Trp	Arg	Ala	Glu	Thr	Asp	Pro	Ile	Arg
		245						250					255		
Glu	Arg	Arg	Phe	Asp	Ala	Val	Glu	Phe	Arg	Val	Ala	Met	Gly	Gly	Pro
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Arg	Glu	Leu	Ala	Asp	Arg	Leu	Ala	Ala	Asp	Asp	Ala	Asp	Leu	Pro	Trp
	275					280					285				
Gly	Val	Pro	Ile	Gly	Pro	Val	Pro	Gly	Gln	Arg	Leu	Asp	Pro	Cys	Leu
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Val	Phe	Asn	Leu	Arg	Asp	Pro	Ala	Asn	Pro	Ala	Val	Ala	Asp	Ala	Ala
305				310					315					320	
Val	Arg	Arg	Val	Val	Ala	Gly	Ala	Val	Asp	Arg	Ala	Ala	Leu	Val	Arg
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Ile	Ala	Arg	Ala	Ala	Asp	Pro	Trp	Ser	Glu	Val	Arg	Ala	Ala	His	Thr
		340					345						350		

Val	Val	Pro	Pro	Gly	Asn	Asp	Gly	His	Arg	Gln	Pro	Asp	Pro	Leu	Thr
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Asp	Pro	Ile	Pro	Asp	Ala	Asp	Ala	Asp	Pro	Arg	Glu	Arg	Leu	Ala	Ala
	370					375					380				
Ala	Gly	His	Pro	Asp	Gly	Leu	Thr	Leu	Thr	Ala	Val	His	Pro	Asp	Thr
385					390					395					400
Ala	Glu	Asp	Leu	Ala	Leu	Ala	Arg	Ser	Trp	Ala	Ala	Asp	Leu	Gly	Ala
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Ala	Gly	Ile	Asp	Val	Arg	Leu	Val	Ala	Leu	Asp	Asp	Ala	Asn	His	Arg
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Ala	Leu	Leu	Ala	Ala	Thr	Gly	Asp	Ala	Pro	Gly	Leu	Arg	Trp	Asp	Leu
	435					440						445			
Ala	Thr	Ala	Thr	Phe	Thr	Ala	Pro	Trp	Ala	Tyr	Gly	Asn	Ala	Arg	Val
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Phe	Leu	Gln	Pro	Leu	Val	Gly	Glu	Gly	Pro	Gly	Asn	Pro	Gly	Gly	Tyr
465					470					475					480
Arg	Asp	Pro	Gly	Val	Asp	Arg	Val	Val	Glu	Arg	Ala	Leu	Asp	Ala	Ala
			485						490					495	
Asp	Pro	Arg	Glu	Ala	Val	Ala	Leu	Trp	Gln	Glu	Val	Glu	Arg	Arg	Leu
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Leu	Ala	Asp	Ala	Ala	Val	Val	Pro	Leu	Leu	Phe	Arg	Arg	Ala	Thr	Asp
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ggg	ctg	cgg	atg	ggt	cgg	ctc	gtc	gag	ggc	tac	gtc	gac	tgc	tgg	ttc	96
Gly	Leu	Arg	Met	Gly	Arg	Leu	Val	Glu	Gly	Tyr	Val	Asp	Cys	Trp	Phe	
			20						25				30			
ggc	gac	cgg	gcc	ctc	gcc	gag	cgg	gtc	gcc	gcg	gag	ccg	gcg	ccg	gac	144
Gly	Asp	Arg	Ala	Leu	Ala	Glu	Arg	Val	Ala	Ala	Glu	Pro	Ala	Pro	Asp	
			35					40				45				
ccg	gcg	gag	ctg	gcc	gga	cag	gcc	cgc	gac	ctg	ctg	cgc	cgc	ctg	ggc	192
Pro	Ala	Glu	Leu	Ala	Gly	Gln	Ala	Arg	Asp	Leu	Leu	Arg	Arg	Leu	Gly	
			50				55					60				
gac	gcg	gac	ctc	gac	gcg	gag	cgg	cgg	cgg	ttc	ctc	gcc	gcg	cag	ctg	240
Asp	Ala	Asp	Leu	Asp	Ala	Glu	Arg	Arg	Arg	Phe	Leu	Ala	Ala	Gln	Leu	
			65				70				75				80	

acc gcg gtg gag tgc gcg gcc cgg cgg gcg gcg ggt gag cag atc ggc	288
Thr Ala Val Glu Cys Ala Ala Arg Arg Ala Ala Gly Glu Gln Ile Gly	
85 90 95	
ttc ctg gcc gag gtg gag acc tac ttc gac gtc gag gtg cgc ctc ggc	336
Phe Leu Ala Glu Val Glu Thr Tyr Phe Asp Val Glu Val Arg Leu Gly	
100 105 110	
gac ccg gac cgg tac gcc gcc gcg cac gac gcc atc gac gcg ctg ctg	384
Asp Pro Asp Arg Tyr Ala Ala Ala His Asp Ala Ile Asp Ala Leu Leu	
115 120 125	
ccg ggc acc ggc ccg ctg atg gac aag gtc gag gcg ttc tac gcc cgc	432
Pro Gly Thr Gly Pro Leu Met Asp Lys Val Glu Ala Phe Tyr Ala Arg	
130 135 140	
aac gtg gtg ccg ccg gag cgg ctg ggc cac gcc gtg cgg gcc gtc gcc	480
Asn Val Val Pro Pro Glu Arg Leu Gly His Ala Val Arg Ala Val Ala	
145 150 155 160	
gac gcg ctg cgc gcc cgt gcc cgg ccg atg ctc ggg ctg ccc gag gcc	528
Asp Ala Leu Arg Ala Arg Ala Arg Pro Met Leu Gly Leu Pro Glu Ala	
165 170 175	
gag cgg gtc gac atc gag gtg gtc cgc gac cgg ccg tgg aac gcg ttc	576
Glu Arg Val Asp Ile Glu Val Val Arg Asp Arg Pro Trp Asn Ala Phe	
180 185 190	
aac cgg tac cac ggc ggc ttc cgt tcc acg gtg acg ctg aac gag acg	624
Asn Arg Tyr His Gly Gly Phe Arg Ser Thr Val Thr Leu Asn Glu Thr	
195 200 205	
gcc ggc cgg acc atc gcc gtg ctg ccg ctg atg gcc acc cac gag gcg	672
Ala Gly Arg Thr Ile Ala Val Leu Pro Leu Met Ala Thr His Glu Ala	
210 215 220	
tac ccg ggc cac cac acc gag cac tgc ctc aag gag gcc ggg ctg gtg	720
Tyr Pro Gly His His Thr Glu His Cys Leu Lys Glu Ala Gly Leu Val	
225 230 235 240	
ctc gac cgg ggc tgg gac gag cac cgc atc gcc ctg gtc aac acc ccg	768
Leu Asp Arg Gly Trp Asp Glu His Arg Ile Ala Leu Val Asn Thr Pro	
245 250 255	
cag tgc ctg gtg gcg gag ggc acc gcc gag cac gcc gcg gcg gcg ctg	816
Gln Cys Leu Val Ala Glu Gly Thr Ala Glu His Ala Ala Ala Ala Leu	
260 265 270	
ctc ggg ccc ggc tgg gga cgg tgg acc acc gag gtg ctg gcc ggc gag	864
Leu Gly Pro Gly Trp Gly Arg Trp Thr Thr Glu Val Leu Ala Gly Glu	
275 280 285	
ggg gtg ccc gtc gag ggc gac ctc gtc gag cgg atg gtg ggg ctc gtc	912
Gly Val Pro Val Glu Gly Asp Leu Val Glu Arg Met Val Gly Leu Val	
290 295 300	
aac gag ctg atg ccg gcc cgg cag gac gcg gcg atc ctg ctg cac gac	960
Asn Glu Leu Met Pro Ala Arg Gln Asp Ala Ala Ile Leu Leu His Asp	



305	310	315	320	
cgg ggg gcg tgc atc gac gac gcg gtg gag cac ctg cac cgg tgg ctg				1008
Arg Gly Ala Ser Ile Asp Asp Ala Val Glu His Leu His Arg Trp Leu				
325		330	335	
ctg ctg ccg cgg gac cgg gcc gag cag atc gcc acc ttc ctg acc gac				1056
Leu Leu Pro Arg Asp Arg Ala Glu Gln Ile Ala Thr Phe Leu Thr Asp				
340	345		350	
ccg ctg tgg cgg gcc tac tcc gtg acg tac atc gag ggg gcc cgg ctg				1104
Pro Leu Trp Arg Ala Tyr Ser Val Thr Tyr Ile Glu Gly Ala Arg Leu				
355	360		365	
gtc ggc ggg tgg ctc gcc gcc cgg ccg gcc ggc gag ccg ctc gtc gcg				1152
Val Gly Gly Trp Leu Ala Ala Arg Pro Ala Gly Glu Pro Leu Val Ala				
370	375		380	
cgg tac cgc acc ctg ctg gcg gag cag ctc ctt ccc gcg cag ctc cgc				1200
Arg Tyr Arg Thr Leu Leu Ala Glu Gln Leu Leu Pro Ala Gln Leu Arg				
385	390	395	400	
gac ggc acg gtc ccc gcg ggc gcg ccg ccc gtg ccc gcg gcc cgc tga				1248
Asp Gly Thr Val Pro Ala Gly Ala Pro Pro Val Pro Ala Ala Arg *				
	405	410	415	

<210> 24  
 <211> 415  
 <212> PRT  
 <213> Bacteria

<400> 24

Val Thr Gly Ala Ala Ala Asp Ala Val Val Ala Asp Tyr Leu Ala Leu			
1	5	10	15
Gly Leu Arg Met Gly Arg Leu Val Glu Gly Tyr Val Asp Cys Trp Phe			
20	25	30	
Gly Asp Arg Ala Leu Ala Glu Arg Val Ala Ala Glu Pro Ala Pro Asp			
35	40	45	
Pro Ala Glu Leu Ala Gly Gln Ala Arg Asp Leu Leu Arg Arg Leu Gly			
50	55	60	
Asp Ala Asp Leu Asp Ala Glu Arg Arg Arg Phe Leu Ala Ala Gln Leu			
65	70	75	80
Thr Ala Val Glu Cys Ala Ala Arg Arg Ala Ala Gly Glu Gln Ile Gly			
85	90	95	
Phe Leu Ala Glu Val Glu Thr Tyr Phe Asp Val Glu Val Arg Leu Gly			
100	105	110	
Asp Pro Asp Arg Tyr Ala Ala Ala His Asp Ala Ile Asp Ala Leu Leu			
115	120	125	
Pro Gly Thr Gly Pro Leu Met Asp Lys Val Glu Ala Phe Tyr Ala Arg			
130	135	140	
Asn Val Val Pro Pro Glu Arg Leu Gly His Ala Val Arg Ala Val Ala			
145	150	155	160
Asp Ala Leu Arg Ala Arg Ala Arg Pro Met Leu Gly Leu Pro Glu Ala			
165	170	175	
Glu Arg Val Asp Ile Glu Val Val Arg Asp Arg Pro Trp Asn Ala Phe			
180	185	190	

```

Asn Arg Tyr His Gly Gly Phe Arg Ser Thr Val Thr Leu Asn Glu Thr
  195                200                205
Ala Gly Arg Thr Ile Ala Val Leu Pro Leu Met Ala Thr His Glu Ala
  210                215                220
Tyr Pro Gly His His Thr Glu His Cys Leu Lys Glu Ala Gly Leu Val
  225                230                235                240
Leu Asp Arg Gly Trp Asp Glu His Arg Ile Ala Leu Val Asn Thr Pro
  245                250                255
Gln Cys Leu Val Ala Glu Gly Thr Ala Glu His Ala Ala Ala Ala Leu
  260                265                270
Leu Gly Pro Gly Trp Gly Arg Trp Thr Thr Glu Val Leu Ala Gly Glu
  275                280                285
Gly Val Pro Val Glu Gly Asp Leu Val Glu Arg Met Val Gly Leu Val
  290                295                300
Asn Glu Leu Met Pro Ala Arg Gln Asp Ala Ala Ile Leu Leu His Asp
  305                310                315                320
Arg Gly Ala Ser Ile Asp Asp Ala Val Glu His Leu His Arg Trp Leu
  325                330                335
Leu Leu Pro Arg Asp Arg Ala Glu Gln Ile Ala Thr Phe Leu Thr Asp
  340                345                350
Pro Leu Trp Arg Ala Tyr Ser Val Thr Tyr Ile Glu Gly Ala Arg Leu
  355                360                365
Val Gly Gly Trp Leu Ala Ala Arg Pro Ala Gly Glu Pro Leu Val Ala
  370                375                380
Arg Tyr Arg Thr Leu Leu Ala Glu Gln Leu Leu Pro Ala Gln Leu Arg
  385                390                395                400
Asp Gly Thr Val Pro Ala Gly Ala Pro Pro Val Pro Ala Ala Arg
  405                410                415

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<210> 25
<211> 1194
<212> DNA
<213> Bacteria

<220>
<221> CDS
<222> (1)...(1194)

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<400> 25
atg gcc cac ctc ctg atc gtc aac gtc gcc agc cac ggc ctg atc ctg      48
Met Ala His Leu Leu Ile Val Asn Val Ala Ser His Gly Leu Ile Leu
  1                5                10                15

ccc acc ctc acc gtg gtc acc gag ctg gtc cgg cgc ggg cac cgg gtc      96
Pro Thr Leu Thr Val Val Thr Glu Leu Val Arg Arg Gly His Arg Val
  20                25                30

agc tac gtc acc gcc ggc ggg ttc gcg gag ccg gtc cgt gcc gcc ggc      144
Ser Tyr Val Thr Ala Gly Gly Phe Ala Glu Pro Val Arg Ala Ala Gly
  35                40                45

gcg acg gtg gtg ccc tac cag tcg gag atc atc gac gcg gac gcc gcc      192
Ala Thr Val Val Pro Tyr Gln Ser Glu Ile Ile Asp Ala Asp Ala Ala
  50                55                60

gag gtg ttc ggc tcg gac gac ctc ggc gtc cgt ccc cac ctg atg tac      240
Glu Val Phe Gly Ser Asp Asp Leu Gly Val Arg Pro His Leu Met Tyr

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65	70	75	80	
ctg cgg gag aac gtc tcg gtg ctc cgg gcc acc gcc gag gcg ctc gac				288
Leu Arg Glu Asn Val Ser Val Leu Arg Ala Thr Ala Glu Ala Leu Asp	85	90	95	
ggc gac gtg ccg gac ctg gtc ctc tac gac gac ttc ccg ttc atc gcc				336
Gly Asp Val Pro Asp Leu Val Leu Tyr Asp Asp Phe Pro Phe Ile Ala	100	105	110	
ggg cag ttg ctg gcc gcc cgc tgg cgg cgg ccg gcc gtc cgg ctc agc				384
Gly Gln Leu Leu Ala Ala Arg Trp Arg Arg Pro Ala Val Arg Leu Ser	115	120	125	
gcg gcg ttc gcg tcg aac gag cac tac tcg ttc tcc cag gac atg gtc				432
Ala Ala Phe Ala Ser Asn Glu His Tyr Ser Phe Ser Gln Asp Met Val	130	135	140	
acc ctg gcc ggc acg atc gac ccg ctc gac ctg ccg gtg ttc cgc gac				480
Thr Leu Ala Gly Thr Ile Asp Pro Leu Asp Leu Pro Val Phe Arg Asp	145	150	155	160
acc ctg cgg gac ctg ctc gcc gag cac ggc ctg tcc ccg tcg gtc gtg				528
Thr Leu Arg Asp Leu Leu Ala Glu His Gly Leu Ser Arg Ser Val Val	165	170	175	
gac tgc tgg aac cac gtg gag caa ctc aac ctg gtc ttc gtc ccg aag				576
Asp Cys Trp Asn His Val Glu Gln Leu Asn Leu Val Phe Val Pro Lys	180	185	190	
gcg ttc cag atc gcc ggc gac acc ttc gac gac cgc ttc gtc ttc gtc				624
Ala Phe Gln Ile Ala Gly Asp Thr Phe Asp Asp Arg Phe Val Phe Val	195	200	205	
ggg ccg tgc ttc gac gac cgg cgg ttc ctc ggc gag tgg acc cgc ccg				672
Gly Pro Cys Phe Asp Asp Arg Arg Phe Leu Gly Glu Trp Thr Arg Pro	210	215	220	
gcc gac gac ctg ccg gtg gtg ctg gtg tcg ctc ggc acc acc ttc aac				720
Ala Asp Asp Leu Pro Val Val Leu Val Ser Leu Gly Thr Thr Phe Asn	225	230	235	240
gac cgg ccc gga ttc ttc cgc gac tgc gcg ccg gcg ttc gac ggc cag				768
Asp Arg Pro Gly Phe Phe Arg Asp Cys Ala Arg Ala Phe Asp Gly Gln	245	250	255	
ccg tgg cac gtg gtg atg acg ctg ggc ggc cag gtc gac ccg gcg gct				816
Pro Trp His Val Val Met Thr Leu Gly Gly Gln Val Asp Pro Ala Ala	260	265	270	
ctc ggc gac ctg ccc ccc aac gtg gag gcg cac cgc tgg gtc ccg cac				864
Leu Gly Asp Leu Pro Pro Asn Val Glu Ala His Arg Trp Val Pro His	275	280	285	
gtg aag gtg ctc gaa cag gcg acg gtc tgc gtg acg cac ggc ggc atg				912
Val Lys Val Leu Glu Gln Ala Thr Val Cys Val Thr His Gly Gly Met	290	295	300	



Gly Pro Cys Phe Asp Asp Arg Arg Phe Leu Gly Glu Trp Thr Arg Pro  
 210 215 220  
 Ala Asp Asp Leu Pro Val Val Leu Val Ser Leu Gly Thr Thr Phe Asn  
 225 230 235 240  
 Asp Arg Pro Gly Phe Phe Arg Asp Cys Ala Arg Ala Phe Asp Gly Gln  
 245 250 255  
 Pro Trp His Val Val Met Thr Leu Gly Gly Gln Val Asp Pro Ala Ala  
 260 265 270  
 Leu Gly Asp Leu Pro Pro Asn Val Glu Ala His Arg Trp Val Pro His  
 275 280 285  
 Val Lys Val Leu Glu Gln Ala Thr Val Cys Val Thr His Gly Gly Met  
 290 295 300  
 Gly Thr Leu Met Glu Ala Leu Tyr Trp Gly Arg Pro Leu Val Val Val  
 305 310 315 320  
 Pro Gln Ser Phe Asp Val Gln Pro Met Ala Arg Arg Val Asp Gln Leu  
 325 330 335  
 Gly Leu Gly Ala Val Leu Pro Gly Glu Lys Ala Asp Gly Asp Thr Leu  
 340 345 350  
 Leu Ala Ala Val Gly Ala Val Ala Ala Asp Pro Ala Leu Leu Ala Arg  
 355 360 365  
 Val Glu Ala Met Arg Gly His Val Arg Arg Ala Gly Gly Ala Ala Arg  
 370 375 380  
 Ala Ala Asp Ala Val Glu Ala Tyr Leu Ala Arg Ala Arg  
 385 390 395

<210> 27  
 <211> 993  
 <212> DNA  
 <213> Bacteria  
  
 <220>  
 <221> CDS  
 <222> (1)...(993)

<400> 27  
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 Val Ser Ser Leu His Val Arg Leu Gly Arg Thr Gly Leu Arg Val Ser  
 1 5 10 15  
  
 cgg gtc gcc atc ggg acc gtc aac ttc ggc ggc cgg gtc gac gag gcc 96  
 Arg Val Ala Ile Gly Thr Val Asn Phe Gly Gly Arg Val Asp Glu Ala  
 20 25 30  
  
 gac gcc cac cgg ctg ctc gac cac gcc gtc gcg cag ggg gtc aac ctg 144  
 Asp Ala His Arg Leu Leu Asp His Ala Val Ala Gln Gly Val Asn Leu  
 35 40 45  
  
 gtc gac acc gcc gac atc tac ggc tgg cgg gtg cac cgg ggc tgg acc 192  
 Val Asp Thr Ala Asp Ile Tyr Gly Trp Arg Val His Arg Gly Trp Thr  
 50 55 60  
  
 gag gag atg atc ggg cgc tgg ctc gcc aag gac ccg gcc cgg cgg gac 240  
 Glu Glu Met Ile Gly Arg Trp Leu Ala Lys Asp Pro Ala Arg Arg Asp  
 65 70 75 80  
  
 gag gtg gtc ctc gcg acc aag gtc ggc aat ccc atg ggg gac ggc ccc 288  
 Glu Val Val Leu Ala Thr Lys Val Gly Asn Pro Met Gly Asp Gly Pro

aac gcc cgg ggc ctg tgc gcc cga cac gtc gtc gcc gcc tgc gag gcg	336
Asn Ala Arg Gly Leu Ser Ala Arg His Val Val Ala Ala Cys Glu Ala	
100 105 110	
tcg ctg cgc cgg ctc cag acc gac gcc atc gac ctc tac cag atg cac	384
Ser Leu Arg Arg Leu Gln Thr Asp Ala Ile Asp Leu Tyr Gln Met His	
115 120 125	
cac gtc gac cgg gag gtc ggc tgg gac gag atc tgg cag gcc atg gag	432
His Val Asp Arg Glu Val Gly Trp Asp Glu Ile Trp Gln Ala Met Glu	
130 135 140	
cag ctc gtc cgg cag ggc aag gtc cgc tac gtc ggg tcc tgc aac ttc	480
Gln Leu Val Arg Gln Gly Lys Val Arg Tyr Val Gly Ser Ser Asn Phe	
145 150 155 160	
gcc ggc tgg gac ctg gtg agc gcc cag gag gcc gcg cgc cgg cac cgg	528
Ala Gly Trp Asp Leu Val Ser Ala Gln Glu Ala Ala Arg Arg His Arg	
165 170 175	
ctg ctc ggg ctg gcc agc gag cag tgc gtc tac aac ctg gtc agc cgg	576
Leu Leu Gly Leu Ala Ser Glu Gln Cys Val Tyr Asn Leu Val Ser Arg	
180 185 190	
tac gtc gaa ctg gag gtg ctc ccc gcc gcc gtc gcc gag ggc atc ggg	624
Tyr Val Glu Leu Glu Val Leu Pro Ala Ala Val Ala Glu Gly Ile Gly	
195 200 205	
gtg ctc gtc tgg tgc ccg ctg cac ggc ggg ctg ctc ggc ggc gtg ctg	672
Val Leu Val Trp Ser Pro Leu His Gly Gly Leu Leu Gly Gly Val Leu	
210 215 220	
cgg aag ctg gcc gac ggc acc gcg gtc aag tcc gcg cag gga cgg gcc	720
Arg Lys Leu Ala Asp Gly Thr Ala Val Lys Ser Ala Gln Gly Arg Ala	
225 230 235 240	
gcc gag gcg gtc gag cgg cac cgc gcg aca ctc gcc gcg tac gag acg	768
Ala Glu Ala Val Glu Arg His Arg Ala Thr Leu Ala Ala Tyr Glu Thr	
245 250 255	
ttc tgc gcc gag gcc ggc cgc gac ccg gcg gag gtc ggc atg gcc tgg	816
Phe Cys Ala Glu Ala Gly Arg Asp Pro Ala Glu Val Gly Met Ala Trp	
260 265 270	
gtg ctg cac cgc ccg gcg gtg acc gcc gcg gtc gtc ggt ccg cgt acc	864
Val Leu His Arg Pro Ala Val Thr Ala Ala Val Val Gly Pro Arg Thr	
275 280 285	
ccc gaa cac ctg gac ggc gcc ctg cgg gcc ctg cac cgg ccg ctg tgc	912
Pro Glu His Leu Asp Gly Ala Leu Arg Ala Leu His Arg Pro Leu Ser	
290 295 300	
gcg gcg gag ctc gcc cgg ctc gac gag ctg ttc ccg ccg ctc ggc cgg	960
Ala Ala Glu Leu Ala Arg Leu Asp Glu Leu Phe Pro Pro Leu Gly Arg	
305 310 315 320	

ggc ggc gcc gcc ccg gac gcc tgg atg tcc tga  
 Gly Gly Ala Ala Pro Asp Ala Trp Met Ser \*  
 325 330

993

<210> 28  
 <211> 330  
 <212> PRT  
 <213> Bacteria

<400> 28  
 Val Ser Ser Leu His Val Arg Leu Gly Arg Thr Gly Leu Arg Val Ser  
 1 5 10 15  
 Arg Val Ala Ile Gly Thr Val Asn Phe Gly Gly Arg Val Asp Glu Ala  
 20 25 30  
 Asp Ala His Arg Leu Leu Asp His Ala Val Ala Gln Gly Val Asn Leu  
 35 40 45  
 Val Asp Thr Ala Asp Ile Tyr Gly Trp Arg Val His Arg Gly Trp Thr  
 50 55 60  
 Glu Glu Met Ile Gly Arg Trp Leu Ala Lys Asp Pro Ala Arg Arg Asp  
 65 70 75 80  
 Glu Val Val Leu Ala Thr Lys Val Gly Asn Pro Met Gly Asp Gly Pro  
 85 90 95  
 Asn Ala Arg Gly Leu Ser Ala Arg His Val Val Ala Ala Cys Glu Ala  
 100 105 110  
 Ser Leu Arg Arg Leu Gln Thr Asp Ala Ile Asp Leu Tyr Gln Met His  
 115 120 125  
 His Val Asp Arg Glu Val Gly Trp Asp Glu Ile Trp Gln Ala Met Glu  
 130 135 140  
 Gln Leu Val Arg Gln Gly Lys Val Arg Tyr Val Gly Ser Ser Asn Phe  
 145 150 155 160  
 Ala Gly Trp Asp Leu Val Ser Ala Gln Glu Ala Ala Arg Arg His Arg  
 165 170 175  
 Leu Leu Gly Leu Ala Ser Glu Gln Cys Val Tyr Asn Leu Val Ser Arg  
 180 185 190  
 Tyr Val Glu Leu Glu Val Leu Pro Ala Ala Val Ala Glu Gly Ile Gly  
 195 200 205  
 Val Leu Val Trp Ser Pro Leu His Gly Gly Leu Leu Gly Gly Val Leu  
 210 215 220  
 Arg Lys Leu Ala Asp Gly Thr Ala Val Lys Ser Ala Gln Gly Arg Ala  
 225 230 235 240  
 Ala Glu Ala Val Glu Arg His Arg Ala Thr Leu Ala Ala Tyr Glu Thr  
 245 250 255  
 Phe Cys Ala Glu Ala Gly Arg Asp Pro Ala Glu Val Gly Met Ala Trp  
 260 265 270  
 Val Leu His Arg Pro Ala Val Thr Ala Ala Val Val Gly Pro Arg Thr  
 275 280 285  
 Pro Glu His Leu Asp Gly Ala Leu Arg Ala Leu His Arg Pro Leu Ser  
 290 295 300  
 Ala Ala Glu Leu Ala Arg Leu Asp Glu Leu Phe Pro Pro Leu Gly Arg  
 305 310 315 320  
 Gly Gly Ala Ala Pro Asp Ala Trp Met Ser  
 325 330

<210> 29  
 <211> 543  
 <212> DNA

<213> Bacteria

<220>

<221> CDS

<222> (1)...(543)

<400> 29

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gga tcc cgg cag gga tat ggg agg atc gcc cac cac aac atc cac ttt      48
Gly Ser Arg Gln Gly Tyr Gly Arg Ile Ala His His Asn Ile His Phe
  1             5             10             15

gga cgg tcc tgg aag ggc acc ttc gat gag gtc atc cgg cgt ggc gag      96
Gly Arg Ser Trp Lys Gly Thr Phe Asp Glu Val Ile Arg Arg Gly Glu
          20             25             30

ctg atg agc gac ccg tcc ctg ctg gtg acc aac ccg agc cgg acg gac     144
Leu Met Ser Asp Pro Ser Leu Leu Val Thr Asn Pro Ser Arg Thr Asp
          35             40             45

ccg tcc gtg gcg ccc gcc ggc cgg cac acc tac tac gtg ctc gcg ccg     192
Pro Ser Val Ala Pro Ala Gly Arg His Thr Tyr Tyr Val Leu Ala Pro
          50             55             60

gtg ccc aac ctc cac cgg gcg ccg ttc gac tgg cgg ggc gac ctc acc     240
Val Pro Asn Leu His Arg Ala Pro Phe Asp Trp Arg Gly Asp Leu Thr
          65             70             75             80

gac cgc tac gcc gac cag ctc gtc ggg acc ctg gag gag cgc ggc tac     288
Asp Arg Tyr Ala Asp Gln Leu Val Gly Thr Leu Glu Glu Arg Gly Tyr
          85             90             95

gtc ggc ttc ggc gcc ggc gtc gag gtg ctg cgg gcg gtc acc ccg gcc     336
Val Gly Phe Gly Ala Gly Val Glu Val Leu Arg Ala Val Thr Pro Ala
          100             105             110

gag tgg gcg gag cag ggg atg gcc gcc ggc acc ccg ttc gcc gcc gcg     384
Glu Trp Ala Glu Gln Gly Met Ala Ala Gly Thr Pro Phe Ala Ala Ala
          115             120             125

cac agc ttc ttc cag acc ggc ccg ttc cgc ccg tcg aac ctg cac cgg     432
His Ser Phe Phe Gln Thr Gly Pro Phe Arg Pro Ser Asn Leu His Arg
          130             135             140

acg ctg ccg aac gtg gtc ttc gtc ggc tcc ggc acc cag ccc ggt gtc     480
Thr Leu Pro Asn Val Val Phe Val Gly Ser Gly Thr Gln Pro Gly Val
          145             150             155             160

ggc gtg ccg atg gtg ctc atc tcc ggc aag ctc gcc gcc ggc cgc atc     528
Gly Val Pro Met Val Leu Ile Ser Gly Lys Leu Ala Ala Gly Arg Ile
          165             170             175

acc ggg aga tcc tga
Thr Gly Arg Ser *
          180
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<210> 30

<211> 180



<212> PRT  
<213> Bacteria

<400> 30  
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1 5 10 15  
Gly Arg Ser Trp Lys Gly Thr Phe Asp Glu Val Ile Arg Arg Gly Glu  
20 25 30  
Leu Met Ser Asp Pro Ser Leu Leu Val Thr Asn Pro Ser Arg Thr Asp  
35 40 45  
Pro Ser Val Ala Pro Ala Gly Arg His Thr Tyr Tyr Val Leu Ala Pro  
50 55 60  
Val Pro Asn Leu His Arg Ala Pro Phe Asp Trp Arg Gly Asp Leu Thr  
65 70 75 80  
Asp Arg Tyr Ala Asp Gln Leu Val Gly Thr Leu Glu Glu Arg Gly Tyr  
85 90 95  
Val Gly Phe Gly Ala Gly Val Glu Val Leu Arg Ala Val Thr Pro Ala  
100 105 110  
Glu Trp Ala Glu Gln Gly Met Ala Ala Gly Thr Pro Phe Ala Ala Ala  
115 120 125  
His Ser Phe Phe Gln Thr Gly Pro Phe Arg Pro Ser Asn Leu His Arg  
130 135 140  
Thr Leu Pro Asn Val Val Phe Val Gly Ser Gly Thr Gln Pro Gly Val  
145 150 155 160  
Gly Val Pro Met Val Leu Ile Ser Gly Lys Leu Ala Ala Gly Arg Ile  
165 170 175  
Thr Gly Arg Ser  
180

<210> 31  
<211> 1362  
<212> DNA  
<213> Bacteria

<220>  
<221> CDS  
<222> (1)...(1362)

<400> 31  
atg ccg ttc ctt ccc gac ccg ggc gaa ccg tcc ccg ctg aag gtg gtc 48  
Met Pro Phe Leu Pro Asp Pro Gly Glu Pro Ser Pro Leu Lys Val Val  
1 5 10 15  
atc gcc ggc gcc ggc tac gtc ggc acc tgt ctc gcc gtc acc ctc gcc 96  
Ile Ala Gly Ala Gly Tyr Val Gly Thr Cys Leu Ala Val Thr Leu Ala  
20 25 30  
ggc cgc ggc gcc gag gtg gtc gcg gtc gac agc gac ccg ggc acc gtc 144  
Gly Arg Gly Ala Glu Val Val Ala Val Asp Ser Asp Pro Gly Thr Val  
35 40 45  
gcg gac ctg cgg gcc ggc cgg tgc cgg ctg ccc gag ccc ggc ctg gcc 192  
Ala Asp Leu Arg Ala Gly Arg Cys Arg Leu Pro Glu Pro Gly Leu Ala  
50 55 60  
ggc gcc gtc cgg gac ctc gcc gcg acc gga cgg ctg acg gcg agc acg 240  
Gly Ala Val Arg Asp Leu Ala Ala Thr Gly Arg Leu Thr Ala Ser Thr

65	70	75	80	
tcg tac gac ccg gtc ggc gcg gcg gac gtg gtg atc gtg acg gtc ggc	288			
Ser Tyr Asp Pro Val Gly Ala Ala Asp Val Val Ile Val Thr Val Gly				
85 90 95				
acc ccg acc gac gcc ggc cac gag atg gtc acc gac cag ctc gtc gcg	336			
Thr Pro Thr Asp Ala Gly His Glu Met Val Thr Asp Gln Leu Val Ala				
100 105 110				
gcg tgc gag cag atc gcc ccg cgg ctg cgc gcc ggg caa ctg gtg atc	384			
Ala Cys Glu Gln Ile Ala Pro Arg Leu Arg Ala Gly Gln Leu Val Ile				
115 120 125				
ctc aag tcg acg gtc tcc ccg ggc acc acc cgg acc ctc gtc gcg ccc	432			
Leu Lys Ser Thr Val Ser Pro Gly Thr Thr Arg Thr Leu Val Ala Pro				
130 135 140				
ctg ctg gag agc ggc ggg ctg gtg cac gag cgc gac ttc ggg ctg gcc	480			
Leu Leu Glu Ser Gly Gly Leu Val His Glu Arg Asp Phe Gly Leu Ala				
145 150 155 160				
ttc tgc ccg gag cgg ctc gcc gag ggg gtg gcg ctg gcg cag gtg cgg	528			
Phe Cys Pro Glu Arg Leu Ala Glu Gly Val Ala Leu Ala Gln Val Arg				
165 170 175				
acg ctg ccg gtg gtg gtg ggt ggg tgc ggc ccg cgc agc gcc gcc gcg	576			
Thr Leu Pro Val Val Val Gly Gly Cys Gly Pro Arg Ser Ala Ala Ala				
180 185 190				
gcc gaa cgg ttc tgg cgg tcc gcg ctc ggc gtc gac gtc cgg cag gtg	624			
Ala Glu Arg Phe Trp Arg Ser Ala Leu Gly Val Asp Val Arg Gln Val				
195 200 205				
ccg tcg gcc gag tcc gcc gag gtg gtc aag ctc gcg acc aac tgg tgg	672			
Pro Ser Ala Glu Ser Ala Glu Val Val Lys Leu Ala Thr Asn Trp Trp				
210 215 220				
atc gac gcg aac gtg gcg atc gcc aac gaa ctc gcc cgg tac tgc gcg	720			
Ile Asp Ala Asn Val Ala Ile Ala Asn Glu Leu Ala Arg Tyr Cys Ala				
225 230 235 240				
gtg ctg ggg gtg gac gtc ctc gac gtg atc ggc gcg gcg aac acc ctg	768			
Val Leu Gly Val Asp Val Leu Asp Val Ile Gly Ala Ala Asn Thr Leu				
245 250 255				
ccc aag ggc agc agc atg gtg aac ctg ctg ctg ccg ggg gtg ggt gtc	816			
Pro Lys Gly Ser Ser Met Val Asn Leu Leu Leu Pro Gly Val Gly Val				
260 265 270				
ggc ggc tcc tgc ctg acg aag gac ccg tgg atg gcg tgg cgg gac ggc	864			
Gly Gly Ser Cys Leu Thr Lys Asp Pro Trp Met Ala Trp Arg Asp Gly				
275 280 285				
cgg gac cgg ggc gtg ccc ctg cgc acg gtc gag acg gcc cgc gcg gtc	912			
Arg Asp Arg Gly Val Pro Leu Arg Thr Val Glu Thr Ala Arg Ala Val				
290 295 300				

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aac gac gac atg ccc cgc cac acc gcc gcc gtc atc gcc gac gag ctg      960
Asn Asp Asp Met Pro Arg His Thr Ala Ala Val Ile Ala Asp Glu Leu
305                      310                      315                      320

gtc aag ctg gga cgg gat cgg aac gac acg acg atc gcc gtg ctc ggc      1008
Val Lys Leu Gly Arg Asp Arg Asn Asp Thr Thr Ile Ala Val Leu Gly
                      325                      330                      335

gcg gcg ttc aag aac gac acc ggc gac gtc cgc aac acc ccg gtg cgc      1056
Ala Ala Phe Lys Asn Asp Thr Gly Asp Val Arg Asn Thr Pro Val Arg
                      340                      345                      350

ggg gtc gtg gcg gcg ctg cgc gac agc ggc ttc cgg gtc cgg atc ttc      1104
Gly Val Val Ala Ala Leu Arg Asp Ser Gly Phe Arg Val Arg Ile Phe
                      355                      360                      365

gac ccg ctg gcc gat ccc gcc gag atc gtc gcc cgg ttc ggc acc gcg      1152
Asp Pro Leu Ala Asp Pro Ala Glu Ile Val Ala Arg Phe Gly Thr Ala
                      370                      375                      380

ccg gcg gcg agc ctg gac gag gcg gtg agc ggg gcg ggc tgc ctg gcc      1200
Pro Ala Ala Ser Leu Asp Glu Ala Val Ser Gly Ala Gly Cys Leu Ala
385                      390                      395                      400

ttc ctc gcc ggg cac cgc cag ttc cac gag ctc gac ttc ggc gcc ctg      1248
Phe Leu Ala Gly His Arg Gln Phe His Glu Leu Asp Phe Gly Ala Leu
                      405                      410                      415

gcc gag cgg gtg gac gag ccc tgc ctg gtc ttc gac ggc cgc atg cac      1296
Ala Glu Arg Val Asp Glu Pro Cys Leu Val Phe Asp Gly Arg Met His
                      420                      425                      430

ctc ccg ccg gcg cgc atc cgc gag ctg cac cgg ttc ggc ttc gcc tac      1344
Leu Pro Pro Ala Arg Ile Arg Glu Leu His Arg Phe Gly Phe Ala Tyr
                      435                      440                      445

cgc ggc att gga agg tga
Arg Gly Ile Gly Arg *
450

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<210> 32
<211> 453
<212> PRT
<213> Bacteria

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Met Pro Phe Leu Pro Asp Pro Gly Glu Pro Ser Pro Leu Lys Val Val
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Ile Ala Gly Ala Gly Tyr Val Gly Thr Cys Leu Ala Val Thr Leu Ala
20                      25                      30
Gly Arg Gly Ala Glu Val Val Ala Val Asp Ser Asp Pro Gly Thr Val
35                      40                      45
Ala Asp Leu Arg Ala Gly Arg Cys Arg Leu Pro Glu Pro Gly Leu Ala
50                      55                      60
Gly Ala Val Arg Asp Leu Ala Ala Thr Gly Arg Leu Thr Ala Ser Thr
65                      70                      75                      80
Ser Tyr Asp Pro Val Gly Ala Ala Asp Val Val Ile Val Thr Val Gly

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														85								90								95			
Thr	Pro	Thr	Asp	Ala	Gly	His	Glu	Met	Val	Thr	Asp	Gln	Leu	Val	Ala																		
														100								105								110			
Ala	Cys	Glu	Gln	Ile	Ala	Pro	Arg	Leu	Arg	Ala	Gly	Gln	Leu	Val	Ile																		
														115								120								125			
Leu	Lys	Ser	Thr	Val	Ser	Pro	Gly	Thr	Thr	Arg	Thr	Leu	Val	Ala	Pro																		
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Leu	Leu	Glu	Ser	Gly	Gly	Leu	Val	His	Glu	Arg	Asp	Phe	Gly	Leu	Ala																		
145															150								155								160		
Phe	Cys	Pro	Glu	Arg	Leu	Ala	Glu	Gly	Val	Ala	Leu	Ala	Gln	Val	Arg																		
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Thr	Leu	Pro	Val	Val	Val	Gly	Gly	Cys	Gly	Pro	Arg	Ser	Ala	Ala	Ala																		
														180								185								190			
Ala	Glu	Arg	Phe	Trp	Arg	Ser	Ala	Leu	Gly	Val	Asp	Val	Arg	Gln	Val																		
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Pro	Ser	Ala	Glu	Ser	Ala	Glu	Val	Val	Lys	Leu	Ala	Thr	Asn	Trp	Trp																		
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Ile	Asp	Ala	Asn	Val	Ala	Ile	Ala	Asn	Glu	Leu	Ala	Arg	Tyr	Cys	Ala																		
225															230								235								240		
Val	Leu	Gly	Val	Asp	Val	Leu	Asp	Val	Ile	Gly	Ala	Ala	Asn	Thr	Leu																		
														245								250								255			
Pro	Lys	Gly	Ser	Ser	Met	Val	Asn	Leu	Leu	Leu	Pro	Gly	Val	Gly	Val																		
														260								265								270			
Gly	Gly	Ser	Cys	Leu	Thr	Lys	Asp	Pro	Trp	Met	Ala	Trp	Arg	Asp	Gly																		
														275								280								285			
Arg	Asp	Arg	Gly	Val	Pro	Leu	Arg	Thr	Val	Glu	Thr	Ala	Arg	Ala	Val																		
														290								295								300			
Asn	Asp	Asp	Met	Pro	Arg	His	Thr	Ala	Ala	Val	Ile	Ala	Asp	Glu	Leu																		
305															310								315								320		
Val	Lys	Leu	Gly	Arg	Asp	Arg	Asn	Asp	Thr	Thr	Ile	Ala	Val	Leu	Gly																		
														325								330								335			
Ala	Ala	Phe	Lys	Asn	Asp	Thr	Gly	Asp	Val	Arg	Asn	Thr	Pro	Val	Arg																		
														340								345								350			
Gly	Val	Val	Ala	Ala	Leu	Arg	Asp	Ser	Gly	Phe	Arg	Val	Arg	Ile	Phe																		
														355								360								365			
Asp	Pro	Leu	Ala	Asp	Pro	Ala	Glu	Ile	Val	Ala	Arg	Phe	Gly	Thr	Ala																		
														370								375								380			
Pro	Ala	Ala	Ser	Leu	Asp	Glu	Ala	Val	Ser	Gly	Ala	Gly	Cys	Leu	Ala																		
385															390								395								400		
Phe	Leu	Ala	Gly	His	Arg	Gln	Phe	His	Glu	Leu	Asp	Phe	Gly	Ala	Leu																		
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Ala	Glu	Arg	Val	Asp	Glu	Pro	Cys	Leu	Val	Phe	Asp	Gly	Arg	Met	His																		
														420								425								430			
Leu	Pro	Pro	Ala	Arg	Ile	Arg	Glu	Leu	His	Arg	Phe	Gly	Phe	Ala	Tyr																		
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Arg	Gly	Ile	Gly	Arg																													
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<211> 843
<212> DNA
<213> Bacteria

<220>
<221> CDS
<222> (1)...(843)
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cgc cgg cac ctg tcg gag ccg ctg cag ctg gcc gac ctg gcc cgg gtt	96
Arg Arg His Leu Ser Glu Pro Leu Gln Leu Ala Asp Leu Ala Arg Val	
20 25 30	
gtc ccc ttc agc ccg ttc cac ttc cac cgg ctg ttc cgc gac gtg acc	144
Val Pro Phe Ser Pro Phe His Phe His Arg Leu Phe Arg Asp Val Thr	
35 40 45	
acg atg acc ccg gcc cgc ttc ctc gcc gcg ctg cgg atg gcg gag gcc	192
Thr Met Thr Pro Ala Arg Phe Leu Ala Ala Leu Arg Met Ala Glu Ala	
50 55 60	
cgc cgg atg ctg ctg cac tcc ggc ctg acg gtg acc gcg atc agc ggc	240
Arg Arg Met Leu Leu His Ser Gly Leu Thr Val Thr Ala Ile Ser Gly	
65 70 75 80	
cac gtc ggc tac acg agc gcg ggg acc ttc acc acc cag ttc tcc cgg	288
His Val Gly Tyr Thr Ser Ala Gly Thr Phe Thr Thr Gln Phe Ser Arg	
85 90 95	
ctg gtc ggc acg tcg ccg ggg cac ttc cgg cag atg tcc cgg ctg ctg	336
Leu Val Gly Thr Ser Pro Gly His Phe Arg Gln Met Ser Arg Leu Leu	
100 105 110	
gcc ggc cgg ccc tgc cac gtc ctg gcg ggc tgg ctg cgc aac gcc gtc	384
Ala Gly Arg Pro Cys His Val Leu Ala Gly Trp Leu Arg Asn Ala Val	
115 120 125	
acg gag gtc acc cga ccc cgg ctg gtg ctg cac gtg ccc gag agc gag	432
Thr Glu Val Thr Arg Pro Arg Leu Val Leu His Val Pro Glu Ser Glu	
130 135 140	
ccc ggc gac ctg gtg ctg gtc ggc ctg cgg gcc gac ggg gag gcc gcg	480
Pro Gly Asp Leu Val Leu Val Gly Leu Arg Ala Asp Gly Glu Ala Ala	
145 150 155 160	
gac gcg tcg acc acg tgg gcg gtg gcg gcc gac ggc gcg cag gtc ccg	528
Asp Ala Ser Thr Thr Trp Ala Val Ala Ala Asp Gly Ala Gln Val Pro	
165 170 175	
gtg gtg gcg cgg ccg ggc ccg tac cag gcc cgg gtc gtg ctg gtc cgg	576
Val Val Ala Arg Pro Gly Pro Tyr Gln Ala Arg Val Val Leu Val Arg	
180 185 190	
ggc gac agc acg ctg acc cgc gcc ctg gtg gac gag gag ccc acc agc	624
Gly Asp Ser Thr Leu Thr Arg Ala Leu Val Asp Glu Glu Pro Thr Ser	
195 200 205	
cat ctg gtc ggc acc gcc gaa ctg gtg ctg ccc cag gac ggc tgc gcg	672
His Leu Val Gly Thr Ala Glu Leu Val Leu Pro Gln Asp Gly Cys Ala	
210 215 220	
gcc gtc ccg gtc acc acc gcg ccg ccg cgg ccg acc gac ccg ccg gcg	720

Ala Val Pro Val Thr Thr Ala Pro Pro Arg Pro Thr Asp Pro Pro Ala  
225 230 235 240

ctg gcc ctc ggc ccg gtg tgc cgg ctc gtc gag acg ttc acg cgg ctg 768  
Leu Ala Leu Gly Pro Val Cys Arg Leu Val Glu Thr Phe Thr Arg Leu  
245 250 255

gcc ggc ccg tcg ggc cgg ccg ggt ccg gcc tgg tcg gcc ggc cgc acc 816  
Ala Gly Pro Ser Gly Arg Pro Gly Pro Ala Trp Ser Ala Gly Arg Thr  
260 265 270

gcg ctg gcc gcg gcg gcc atc gcg tga 843  
Ala Leu Ala Ala Ala Ala Ile Ala \*  
275 280

<210> 34  
<211> 280  
<212> PRT  
<213> Bacteria

<400> 34  
Met Glu Gln Ser Arg Glu Ala Ala Ala Ala Arg Ala Ile Asp Tyr Met  
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20 25 30  
Val Pro Phe Ser Pro Phe His Phe His Arg Leu Phe Arg Asp Val Thr  
35 40 45  
Thr Met Thr Pro Ala Arg Phe Leu Ala Ala Leu Arg Met Ala Glu Ala  
50 55 60  
Arg Arg Met Leu Leu His Ser Gly Leu Thr Val Thr Ala Ile Ser Gly  
65 70 75 80  
His Val Gly Tyr Thr Ser Ala Gly Thr Phe Thr Thr Gln Phe Ser Arg  
85 90 95  
Leu Val Gly Thr Ser Pro Gly His Phe Arg Gln Met Ser Arg Leu Leu  
100 105 110  
Ala Gly Arg Pro Cys His Val Leu Ala Gly Trp Leu Arg Asn Ala Val  
115 120 125  
Thr Glu Val Thr Arg Pro Arg Leu Val Leu His Val Pro Glu Ser Glu  
130 135 140  
Pro Gly Asp Leu Val Leu Val Gly Leu Arg Ala Asp Gly Glu Ala Ala  
145 150 155 160  
Asp Ala Ser Thr Thr Trp Ala Val Ala Ala Asp Gly Ala Gln Val Pro  
165 170 175  
Val Val Ala Arg Pro Gly Pro Tyr Gln Ala Arg Val Val Leu Val Arg  
180 185 190  
Gly Asp Ser Thr Leu Thr Arg Ala Leu Val Asp Glu Glu Pro Thr Ser  
195 200 205  
His Leu Val Gly Thr Ala Glu Leu Val Leu Pro Gln Asp Gly Cys Ala  
210 215 220  
Ala Val Pro Val Thr Thr Ala Pro Pro Arg Pro Thr Asp Pro Pro Ala  
225 230 235 240  
Leu Ala Leu Gly Pro Val Cys Arg Leu Val Glu Thr Phe Thr Arg Leu  
245 250 255  
Ala Gly Pro Ser Gly Arg Pro Gly Pro Ala Trp Ser Ala Gly Arg Thr  
260 265 270  
Ala Leu Ala Ala Ala Ala Ile Ala  
275 280

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 <211> 1209  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(1209)

<400> 35

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1				5					10					15		
cgg	cgt	gac	ccc	tac	cgg	tcc	tac	cac	tgg	ctg	ctg	cgg	cac	gac	ccg	96
Arg	Arg	Asp	Pro	Tyr	Pro	Ser	Tyr	His	Trp	Leu	Leu	Arg	His	Asp	Pro	
			20					25					30			
gtg	cac	cgt	ggc	gcc	cac	cgg	gtc	tgg	tac	gtc	tcc	cgc	ttc	gcg	gac	144
Val	His	Arg	Gly	Ala	His	Arg	Val	Trp	Tyr	Val	Ser	Arg	Phe	Ala	Asp	
			35				40					45				
gtg	cgc	gcg	gtg	ctc	ggc	gac	gag	cgc	ttc	gcc	cgg	acc	ggc	atc	cgc	192
Val	Arg	Ala	Val	Leu	Gly	Asp	Glu	Arg	Phe	Ala	Arg	Thr	Gly	Ile	Arg	
	50					55					60					
cgg	ttc	tgg	acc	gac	ctc	gtc	ggg	ccc	ggg	ctg	ctc	gcc	gag	atc	gtc	240
Arg	Phe	Trp	Thr	Asp	Leu	Val	Gly	Pro	Gly	Leu	Leu	Ala	Glu	Ile	Val	
65					70				75						80	
ggc	gac	atc	atc	ctg	ttc	cag	gac	gag	ccc	gac	cac	ggc	cgg	ctg	cgc	288
Gly	Asp	Ile	Ile	Leu	Phe	Gln	Asp	Glu	Pro	Asp	His	Gly	Arg	Leu	Arg	
				85				90					95			
ggg	gtg	gtc	ggc	ccg	gcg	ttc	tgg	ccg	tcc	gcg	ctg	cgc	cgg	ctg	gaa	336
Gly	Val	Val	Gly	Pro	Ala	Phe	Ser	Pro	Ser	Ala	Leu	Arg	Arg	Leu	Glu	
			100					105					110			
ccg	gtg	atc	gcc	ggc	acc	gtg	gac	gac	ctg	ctg	cgg	ccc	gcc	ctg	gcc	384
Pro	Val	Ile	Ala	Gly	Thr	Val	Asp	Asp	Leu	Leu	Arg	Pro	Ala	Leu	Ala	
		115					120					125				
cgg	ggc	gcg	atg	gac	gtg	gtc	gac	gag	ctg	gcg	tac	ccg	ctg	gcg	ctg	432
Arg	Gly	Ala	Met	Asp	Val	Val	Asp	Glu	Leu	Ala	Tyr	Pro	Leu	Ala	Leu	
	130					135					140					
cgc	gcg	gtc	ctc	ggc	ctg	ctc	ggc	ctg	ccc	gcc	gcc	gac	tgg	ggg	gcg	480
Arg	Ala	Val	Leu	Gly	Leu	Leu	Gly	Leu	Pro	Ala	Ala	Asp	Trp	Gly	Ala	
145					150				155					160		
gtc	ggg	cgc	tgg	tgg	cgc	gac	gtg	gga	cgg	acc	ctg	gac	cgg	ggc	gcc	528
Val	Gly	Arg	Trp	Ser	Arg	Asp	Val	Gly	Arg	Thr	Leu	Asp	Arg	Gly	Ala	
				165				170						175		
agc	gcc	gag	gac	atg	cgc	cgc	ggc	cac	gcg	gcg	atc	gcc	gag	ttc	gcc	576
Ser	Ala	Glu	Asp	Met	Arg	Arg	Gly	His	Ala	Ala	Ile	Ala	Glu	Phe	Ala	
				180				185					190			

gac tac gtg gag cgg gcc ctc gcg agg cgg cgg cgt gag ggc ggc gag	624
Asp Tyr Val Glu Arg Ala Leu Ala Arg Arg Arg Arg Glu Gly Gly Glu	
195 200 205	
gac ctg ctg gcg ttg atg ctc gac gcc cac gac cgc ggc ctg atg agt	672
Asp Leu Leu Ala Leu Met Leu Asp Ala His Asp Arg Gly Leu Met Ser	
210 215 220	
cgc aac gag atc gtc agc acg gtg gtc acg ttc atc ttc acc ggc cac	720
Arg Asn Glu Ile Val Ser Thr Val Val Thr Phe Ile Phe Thr Gly His	
225 230 235 240	
gag acg gtg gcc agc cag gtg ggc aac gcc gtg ctg agc ctg ctg gcg	768
Glu Thr Val Ala Ser Gln Val Gly Asn Ala Val Leu Ser Leu Leu Ala	
245 250 255	
cac ccg gac cag ctc gac ctg ctc cgg cgc cgg ccg gac ctg ctg gcc	816
His Pro Asp Gln Leu Asp Leu Leu Arg Arg Arg Pro Asp Leu Leu Ala	
260 265 270	
cag gcc gtc gag gag tgc ctg cgg tac gac ccg tcg gtg cag tcc aac	864
Gln Ala Val Glu Glu Cys Leu Arg Tyr Asp Pro Ser Val Gln Ser Asn	
275 280 285	
acc cgg cag ctc gac gtc gac gtg gag ctg cgc ggt cgg cgg ctg cgc	912
Thr Arg Gln Leu Asp Val Asp Val Glu Leu Arg Gly Arg Arg Leu Arg	
290 295 300	
cgc gac gac gtc gtg gtc gtc ctg gcc ggc gcg gcg aac cgg gac ccg	960
Arg Asp Asp Val Val Val Val Leu Ala Gly Ala Ala Asn Arg Asp Pro	
305 310 315 320	
cgg cgg tac gac cgg ccc gac gat ttc gac atc gag cgg gat ccg gtc	1008
Arg Arg Tyr Asp Arg Pro Asp Asp Phe Asp Ile Glu Arg Asp Pro Val	
325 330 335	
ccg tcg atg tcc ttc ggc gcg ggg atg cgc tac tgc ctc ggg tcc tac	1056
Pro Ser Met Ser Phe Gly Ala Gly Met Arg Tyr Cys Leu Gly Ser Tyr	
340 345 350	
ctc gcc cgt acg cag ctg cgc gcc gcg gtg gcc gcc ctg gcc cga ctg	1104
Leu Ala Arg Thr Gln Leu Arg Ala Ala Val Ala Ala Leu Ala Arg Leu	
355 360 365	
ccg ggc ctg cgg ctg ggc tgc gcg tcg gac gcc ctg gcc tat cag ccg	1152
Pro Gly Leu Arg Leu Gly Cys Ala Ser Asp Ala Leu Ala Tyr Gln Pro	
370 375 380	
cgc acc atg ttc cgg ggc ctg gcc agc ctg ccg atc gcg ttc acg ccg	1200
Arg Thr Met Phe Arg Gly Leu Ala Ser Leu Pro Ile Ala Phe Thr Pro	
385 390 395 400	
ggc ggt tga	1209
Gly Gly *	



<210> 36  
 <211> 402  
 <212> PRT  
 <213> Bacteria

<400> 36

Val	Leu	Val	Asp	Ala	Val	Thr	Ala	Phe	Asp	Pro	Thr	Asp	Ala	Asp	Val
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			20					25					30		
Val	His	Arg	Gly	Ala	His	Arg	Val	Trp	Tyr	Val	Ser	Arg	Phe	Ala	Asp
		35					40					45			
Val	Arg	Ala	Val	Leu	Gly	Asp	Glu	Arg	Phe	Ala	Arg	Thr	Gly	Ile	Arg
	50					55					60				
Arg	Phe	Trp	Thr	Asp	Leu	Val	Gly	Pro	Gly	Leu	Leu	Ala	Glu	Ile	Val
65					70					75					80
Gly	Asp	Ile	Ile	Leu	Phe	Gln	Asp	Glu	Pro	Asp	His	Gly	Arg	Leu	Arg
				85					90					95	
Gly	Val	Val	Gly	Pro	Ala	Phe	Ser	Pro	Ser	Ala	Leu	Arg	Arg	Leu	Glu
			100					105					110		
Pro	Val	Ile	Ala	Gly	Thr	Val	Asp	Asp	Leu	Leu	Arg	Pro	Ala	Leu	Ala
			115				120						125		
Arg	Gly	Ala	Met	Asp	Val	Val	Asp	Glu	Leu	Ala	Tyr	Pro	Leu	Ala	Leu
	130					135					140				
Arg	Ala	Val	Leu	Gly	Leu	Leu	Gly	Leu	Pro	Ala	Ala	Asp	Trp	Gly	Ala
145					150					155					160
Val	Gly	Arg	Trp	Ser	Arg	Asp	Val	Gly	Arg	Thr	Leu	Asp	Arg	Gly	Ala
				165					170					175	
Ser	Ala	Glu	Asp	Met	Arg	Arg	Gly	His	Ala	Ala	Ile	Ala	Glu	Phe	Ala
			180					185					190		
Asp	Tyr	Val	Glu	Arg	Ala	Leu	Ala	Arg	Arg	Arg	Arg	Glu	Gly	Gly	Glu
	195					200						205			
Asp	Leu	Leu	Ala	Leu	Met	Leu	Asp	Ala	His	Asp	Arg	Gly	Leu	Met	Ser
	210				215						220				
Arg	Asn	Glu	Ile	Val	Ser	Thr	Val	Val	Thr	Phe	Ile	Phe	Thr	Gly	His
225					230					235					240
Glu	Thr	Val	Ala	Ser	Gln	Val	Gly	Asn	Ala	Val	Leu	Ser	Leu	Leu	Ala
				245					250					255	
His	Pro	Asp	Gln	Leu	Asp	Leu	Leu	Arg	Arg	Arg	Pro	Asp	Leu	Leu	Ala
			260					265					270		
Gln	Ala	Val	Glu	Glu	Cys	Leu	Arg	Tyr	Asp	Pro	Ser	Val	Gln	Ser	Asn
		275					280					285			
Thr	Arg	Gln	Leu	Asp	Val	Asp	Val	Glu	Leu	Arg	Gly	Arg	Arg	Leu	Arg
	290					295					300				
Arg	Asp	Asp	Val	Val	Val	Val	Leu	Ala	Gly	Ala	Ala	Asn	Arg	Asp	Pro
305					310					315					320
Arg	Arg	Tyr	Asp	Arg	Pro	Asp	Asp	Phe	Asp	Ile	Glu	Arg	Asp	Pro	Val
				325					330					335	
Pro	Ser	Met	Ser	Phe	Gly	Ala	Gly	Met	Arg	Tyr	Cys	Leu	Gly	Ser	Tyr
			340					345					350		
Leu	Ala	Arg	Thr	Gln	Leu	Arg	Ala	Ala	Val	Ala	Ala	Leu	Ala	Arg	Leu
		355					360					365			
Pro	Gly	Leu	Arg	Leu	Gly	Cys	Ala	Ser	Asp	Ala	Leu	Ala	Tyr	Gln	Pro
	370					375					380				
Arg	Thr	Met	Phe	Arg	Gly	Leu	Ala	Ser	Leu	Pro	Ile	Ala	Phe	Thr	Pro
385					390					395					400
Gly	Gly														

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<210> 37  
 <211> 1263  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
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 ccg gcc gga tcg agc acg gcc ggt ctg ctc gcc cag gag ggc cac cgg 96  
 Pro Ala Gly Ser Ser Thr Ala Gly Leu Leu Ala Gln Glu Gly His Arg  
 20 25 30  
 gtc ctg ctg ctg gag cgc gag aag ttc ccc cgc tac cac atc ggc gag 144  
 Val Leu Leu Leu Glu Arg Glu Lys Phe Pro Arg Tyr His Ile Gly Glu  
 35 40 45  
 tcc ctg atc agc ggc gtc acc ctc acc ctg gac gcg ctc ggc gta cgc 192  
 Ser Leu Ile Ser Gly Val Thr Leu Thr Leu Asp Ala Leu Gly Val Arg  
 50 55 60  
 gag cgg atg gcg gag ctg cgc ttc cag atc aaa cac ggc ggc agc ctg 240  
 Glu Arg Met Ala Glu Leu Arg Phe Gln Ile Lys His Gly Gly Ser Leu  
 65 70 75 80  
 ctg tgg ggg gcc gat cag acc gcc ccg tgg tcg ttc cgg ttc cgg gag 288  
 Leu Trp Gly Ala Asp Gln Thr Ala Pro Trp Ser Phe Arg Phe Arg Glu  
 85 90 95  
 atc cgc gac gcc cgg ttc gac tac tcg tgg cag gtc cgg cgt gcc gaa 336  
 Ile Arg Asp Ala Arg Phe Asp Tyr Ser Trp Gln Val Arg Arg Ala Glu  
 100 105 110  
 ttc gac gcg atg ctg ctg gac cgg gcg cgg gaa ctg ggc gtg gtg gtg 384  
 Phe Asp Ala Met Leu Leu Asp Arg Ala Arg Glu Leu Gly Val Val Val  
 115 120 125  
 gtc gag gga gcc acc gtc cgg ggg ccg ctg acc gac ggc gag cgg gtc 432  
 Val Glu Gly Ala Thr Val Arg Gly Pro Leu Thr Asp Gly Glu Arg Val  
 130 135 140  
 gcg ggc gtc agc tac cag ttc cgg ggt gag gcc gac ccg atc gac gcc 480  
 Ala Gly Val Ser Tyr Gln Phe Arg Gly Glu Ala Asp Pro Ile Asp Ala  
 145 150 155 160  
 cgc gcc gcg atc gtg gtc gac gcg tcg ggg cag cag cgc tgg ctc ggc 528  
 Arg Ala Ala Ile Val Val Asp Ala Ser Gly Gln Gln Arg Trp Leu Gly  
 165 170 175  
 cgg cac ttc ggg ttg gtc tcc tgg cac gac gac ctg cgc aac atg gcg 576  
 Arg His Phe Gly Leu Val Ser Trp His Asp Asp Leu Arg Asn Met Ala  
 180 185 190

gcg tgg agc tac tac gcc ggg gcg ctg cgc tac ccc ggc gat cac gag	624
Ala Trp Ser Tyr Tyr Ala Gly Ala Leu Arg Tyr Pro Gly Asp His Glu	
195 200 205	
ggc gac ctg ctc gtc gag agc tgc gcc cag ggt tgg ctc tgg tac gcg	672
Gly Asp Leu Leu Val Glu Ser Cys Ala Gln Gly Trp Leu Trp Tyr Ala	
210 215 220	
ccg ctg agc ccc acc ctg acc ggg atc ggg tac gtc acc ccg tcg gac	720
Pro Leu Ser Pro Thr Leu Thr Gly Ile Gly Tyr Val Thr Pro Ser Asp	
225 230 235 240	
cgg ttc gcc gag acc ggc ctt ccc ccg gat cag ttg ctg gag aaa cag	768
Arg Phe Ala Glu Thr Gly Leu Pro Pro Asp Gln Leu Leu Glu Lys Gln	
245 250 255	
atc gcg gag tcg aac gag gtc tcc tgg ctc acc gcc ggc gcg cgg cgg	816
Ile Ala Glu Ser Asn Glu Val Ser Trp Leu Thr Ala Gly Ala Arg Arg	
260 265 270	
gtc gac gtc tac cgc acc gcg cgg gac tgg tcg tac gcg tgc agc cag	864
Val Asp Val Tyr Arg Thr Ala Arg Asp Trp Ser Tyr Ala Cys Ser Gln	
275 280 285	
ttc tcc ggg ccg ggc tgg gtg ctg gtc ggt gac gcc gcc gcc ttc atc	912
Phe Ser Gly Pro Gly Trp Val Leu Val Gly Asp Ala Ala Ala Phe Ile	
290 295 300	
gac ccc ctg ctg tcc tcc ggc gtg acg ctg gcg atg cgc ggc gcg ctc	960
Asp Pro Leu Leu Ser Ser Gly Val Thr Leu Ala Met Arg Gly Ala Leu	
305 310 315 320	
agc ctg tcc cgg gcg gtg cac gag gca ctg gcc gcg ccg gag aag gag	1008
Ser Leu Ser Arg Ala Val His Glu Ala Leu Ala Ala Pro Glu Lys Glu	
325 330 335	
cgc cat ctc atg cag gtg tac gag gac cgc tac cgg gac ttc ctc gcc	1056
Arg His Leu Met Gln Val Tyr Glu Asp Arg Tyr Arg Asp Phe Leu Ala	
340 345 350	
gcc ctg ctg gat ctg atc cgg ttc ttc tac gac ggc gcg cac ggc cgc	1104
Ala Leu Leu Asp Leu Ile Arg Phe Phe Tyr Asp Gly Ala His Gly Arg	
355 360 365	
gac gag ttg cac ctg cgc gcc cag gcc atc gtg gac ccg gac cgg ctg	1152
Asp Glu Leu His Leu Arg Ala Gln Ala Ile Val Asp Pro Asp Arg Leu	
370 375 380	
atg cct ccg aag atc tcg ttc gtc tcc ctg ctg tcg ggg ctg gcg cgg	1200
Met Pro Pro Lys Ile Ser Phe Val Ser Leu Leu Ser Gly Leu Ala Arg	
385 390 395 400	
ggc gac gag acg ctc gac cgc agc cct cgg acg gcc att gac cga ccg	1248
Gly Asp Glu Thr Leu Asp Arg Ser Pro Arg Thr Ala Ile Asp Arg Pro	
405 410 415	
tca gac gct ata taa	1263

Ser Asp Ala Ile \*  
420

<210> 38  
<211> 420  
<212> PRT  
<213> Bacteria

<400> 38  
Met Ser His Pro Glu Pro Glu Tyr Asp Val Ile Val Val Gly Gly Gly  
1 5 10 15  
Pro Ala Gly Ser Ser Thr Ala Gly Leu Leu Ala Gln Glu Gly His Arg  
20 25 30  
Val Leu Leu Leu Glu Arg Glu Lys Phe Pro Arg Tyr His Ile Gly Glu  
35 40 45  
Ser Leu Ile Ser Gly Val Thr Leu Thr Leu Asp Ala Leu Gly Val Arg  
50 55 60  
Glu Arg Met Ala Glu Leu Arg Phe Gln Ile Lys His Gly Gly Ser Leu  
65 70 75 80  
Leu Trp Gly Ala Asp Gln Thr Ala Pro Trp Ser Phe Arg Phe Arg Glu  
85 90 95  
Ile Arg Asp Ala Arg Phe Asp Tyr Ser Trp Gln Val Arg Arg Ala Glu  
100 105 110  
Phe Asp Ala Met Leu Leu Asp Arg Ala Arg Glu Leu Gly Val Val Val  
115 120 125  
Val Glu Gly Ala Thr Val Arg Gly Pro Leu Thr Asp Gly Glu Arg Val  
130 135 140  
Ala Gly Val Ser Tyr Gln Phe Arg Gly Glu Ala Asp Pro Ile Asp Ala  
145 150 155 160  
Arg Ala Ala Ile Val Val Asp Ala Ser Gly Gln Gln Arg Trp Leu Gly  
165 170 175  
Arg His Phe Gly Leu Val Ser Trp His Asp Asp Leu Arg Asn Met Ala  
180 185 190  
Ala Trp Ser Tyr Tyr Ala Gly Ala Leu Arg Tyr Pro Gly Asp His Glu  
195 200 205  
Gly Asp Leu Leu Val Glu Ser Cys Ala Gln Gly Trp Leu Trp Tyr Ala  
210 215 220  
Pro Leu Ser Pro Thr Leu Thr Gly Ile Gly Tyr Val Thr Pro Ser Asp  
225 230 235 240  
Arg Phe Ala Glu Thr Gly Leu Pro Pro Asp Gln Leu Leu Glu Lys Gln  
245 250 255  
Ile Ala Glu Ser Asn Glu Val Ser Trp Leu Thr Ala Gly Ala Arg Arg  
260 265 270  
Val Asp Val Tyr Arg Thr Ala Arg Asp Trp Ser Tyr Ala Cys Ser Gln  
275 280 285  
Phe Ser Gly Pro Gly Trp Val Leu Val Gly Asp Ala Ala Ala Phe Ile  
290 295 300  
Asp Pro Leu Leu Ser Ser Gly Val Thr Leu Ala Met Arg Gly Ala Leu  
305 310 315 320  
Ser Leu Ser Arg Ala Val His Glu Ala Leu Ala Ala Pro Glu Lys Glu  
325 330 335  
Arg His Leu Met Gln Val Tyr Glu Asp Arg Tyr Arg Asp Phe Leu Ala  
340 345 350  
Ala Leu Leu Asp Leu Ile Arg Phe Tyr Asp Gly Ala His Gly Arg  
355 360 365  
Asp Glu Leu His Leu Arg Ala Gln Ala Ile Val Asp Pro Asp Arg Leu  
370 375 380

Met Pro Pro Lys Ile Ser Phe Val Ser Leu Leu Ser Gly Leu Ala Arg  
 385 390 395 400  
 Gly Asp Glu Thr Leu Asp Arg Ser Pro Arg Thr Ala Ile Asp Arg Pro  
 405 410 415  
 Ser Asp Ala Ile  
 420

<210> 39  
 <211> 1137  
 <212> DNA  
 <213> B

<220>  
 <221> CDS  
 <222> (1)...(1137)

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 Met Arg Val Leu Phe Val Ser Ser Pro Gly Ile Gly His Leu Phe Pro  
 1 5 10 15  
 ctg atc cag ctc gcc tgg ggc ttc cgc acg gcc ggc cac gac gtg ctg 96  
 Leu Ile Gln Leu Ala Trp Gly Phe Arg Thr Ala Gly His Asp Val Leu  
 20 25 30  
 atc gcg gtc gcc gag cac gcc gac cgg gcc gcc gcc gcg ggc ctg gag 144  
 Ile Ala Val Ala Glu His Ala Asp Arg Ala Ala Ala Ala Gly Leu Glu  
 35 40 45  
 gtc gtc gac gtg gcg ccc gac tac agc gcg gtc aag gtc ttc gag cag 192  
 Val Val Asp Val Ala Pro Asp Tyr Ser Ala Val Lys Val Phe Glu Gln  
 50 55 60  
 gtg gcc aag gac aac ccg cgc ttc gcc gag acc gtc gcc acg cgt ccc 240  
 Val Ala Lys Asp Asn Pro Arg Phe Ala Glu Thr Val Ala Thr Arg Pro  
 65 70 75 80  
 gcg atc gat ctg gag gag tgg ggc gtg cag atc gcg gcg gtg aac cgc 288  
 Ala Ile Asp Leu Glu Glu Trp Gly Val Gln Ile Ala Ala Val Asn Arg  
 85 90 95  
 ccg ctg gtc gac ggg acc atg gcg ctg gtc gac gac tac cgt ccc gac 336  
 Pro Leu Val Asp Gly Thr Met Ala Leu Val Asp Asp Tyr Arg Pro Asp  
 100 105 110  
 ctg gtg gtc tac gag cag ggc gcc acc gtc ggc ctg ctg gcc gcc gac 384  
 Leu Val Val Tyr Glu Gln Gly Ala Thr Val Gly Leu Leu Ala Ala Asp  
 115 120 125  
 cgc gcc ggg gtg ccg gca gtg cag cgc aac cag agc gcc tgg cgg acc 432  
 Arg Ala Gly Val Pro Ala Val Gln Arg Asn Gln Ser Ala Trp Arg Thr  
 130 135 140  
 cgg ggc atg cac cgc tcg atc gcg tcc ttc ctg acc gac ctg atg gac 480  
 Arg Gly Met His Arg Ser Ile Ala Ser Phe Leu Thr Asp Leu Met Asp  
 145 150 155 160

aag cac cag gtc agc ctg ccc gag ccg gtg gcg acg atc gag tcg ttc	528
Lys His Gln Val Ser Leu Pro Glu Pro Val Ala Thr Ile Glu Ser Phe	
165 170 175	
ccg ccg agc ctg ctg ctg gag gcg gag ccc gag ggc tgg ttc atg cgc	576
Pro Pro Ser Leu Leu Leu Glu Ala Glu Pro Glu Gly Trp Phe Met Arg	
180 185 190	
tgg gtg ccg tac ggc ggc ggc gcc gtc ctc ggc gac cgg ctg ccg ccg	624
Trp Val Pro Tyr Gly Gly Gly Ala Val Leu Gly Asp Arg Leu Pro Pro	
195 200 205	
gtg ccc gcc ccg ccc gag gtg gcg atc acc atg ggc acc atc gag ctc	672
Val Pro Ala Arg Pro Glu Val Ala Ile Thr Met Gly Thr Ile Glu Leu	
210 215 220	
cag gcg ttc ggc atc ggc gcc gtg gag ccc atc atc gcc gcc gcc ggc	720
Gln Ala Phe Gly Ile Gly Ala Val Glu Pro Ile Ile Ala Ala Ala Gly	
225 230 235 240	
gag gtg gac gcc gac ttc gtg ctc gcc ctc ggc gac ctc gac atc agc	768
Glu Val Asp Ala Asp Phe Val Leu Ala Leu Gly Asp Leu Asp Ile Ser	
245 250 255	
ccg ctg ggc acg ttg ccg cgc aac gtc cgg gcg gtc ggc tgg acg ccg	816
Pro Leu Gly Thr Leu Pro Arg Asn Val Arg Ala Val Gly Trp Thr Pro	
260 265 270	
ctg cac acc ctg ctg cgt acc tgc acc gcg gtg gtg cac cac ggc ggc	864
Leu His Thr Leu Leu Arg Thr Cys Thr Ala Val Val His His Gly Gly	
275 280 285	
ggc ggc acg gtg atg acc gcc atc gac gcc ggc atc ccg cag ctg ctc	912
Gly Gly Thr Val Met Thr Ala Ile Asp Ala Gly Ile Pro Gln Leu Leu	
290 295 300	
gcc ccg gac ccg cgc gac cag ttc cag cac acc gcc ccg gag gcc gtc	960
Ala Pro Asp Pro Arg Asp Gln Phe Gln His Thr Ala Arg Glu Ala Val	
305 310 315 320	
agc cgg cgc ggc atc ggc ctg gtc agc acg tcg gac aag gtc gac gcg	1008
Ser Arg Arg Gly Ile Gly Leu Val Ser Thr Ser Asp Lys Val Asp Ala	
325 330 335	
gac ctg ctg cgc ccg ctg atc ggg gac gag tcg ctg cgc acc gcg gcc	1056
Asp Leu Leu Arg Arg Leu Ile Gly Asp Glu Ser Leu Arg Thr Ala Ala	
340 345 350	
cgg gag gta cgc gag gag atg gtc gcg ctg ccc acg ccg gcg gag acg	1104
Arg Glu Val Arg Glu Glu Met Val Ala Leu Pro Thr Pro Ala Glu Thr	
355 360 365	
gtg cgg cgc atc gtc gag cgc atc tcg ggt tga	1137
Val Arg Arg Ile Val Glu Arg Ile Ser Gly *	
370 375	

<210> 40

<211> 378  
 <212> PRT  
 <213> Bacteria

<400> 40

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Met Arg Val Leu Phe Val Ser Ser Pro Gly Ile Gly His Leu Phe Pro
 1           5           10           15
Leu Ile Gln Leu Ala Trp Gly Phe Arg Thr Ala Gly His Asp Val Leu
          20           25           30
Ile Ala Val Ala Glu His Ala Asp Arg Ala Ala Ala Ala Gly Leu Glu
          35           40           45
Val Val Asp Val Ala Pro Asp Tyr Ser Ala Val Lys Val Phe Glu Gln
          50           55           60
Val Ala Lys Asp Asn Pro Arg Phe Ala Glu Thr Val Ala Thr Arg Pro
65          70          75          80
Ala Ile Asp Leu Glu Trp Gly Val Gln Ile Ala Ala Val Asn Arg
          85          90          95
Pro Leu Val Asp Gly Thr Met Ala Leu Val Asp Asp Tyr Arg Pro Asp
          100         105         110
Leu Val Val Tyr Glu Gln Gly Ala Thr Val Gly Leu Leu Ala Ala Asp
          115         120         125
Arg Ala Gly Val Pro Ala Val Gln Arg Asn Gln Ser Ala Trp Arg Thr
          130         135         140
Arg Gly Met His Arg Ser Ile Ala Ser Phe Leu Thr Asp Leu Met Asp
145         150         155         160
Lys His Gln Val Ser Leu Pro Glu Pro Val Ala Thr Ile Glu Ser Phe
          165         170         175
Pro Pro Ser Leu Leu Leu Glu Ala Glu Pro Glu Gly Trp Phe Met Arg
          180         185         190
Trp Val Pro Tyr Gly Gly Gly Ala Val Leu Gly Asp Arg Leu Pro Pro
          195         200         205
Val Pro Ala Arg Pro Glu Val Ala Ile Thr Met Gly Thr Ile Glu Leu
          210         215         220
Gln Ala Phe Gly Ile Gly Ala Val Glu Pro Ile Ile Ala Ala Ala Gly
225         230         235         240
Glu Val Asp Ala Asp Phe Val Leu Ala Leu Gly Asp Leu Asp Ile Ser
          245         250         255
Pro Leu Gly Thr Leu Pro Arg Asn Val Arg Ala Val Gly Trp Thr Pro
          260         265         270
Leu His Thr Leu Leu Arg Thr Cys Thr Ala Val Val His His Gly Gly
          275         280         285
Gly Gly Thr Val Met Thr Ala Ile Asp Ala Gly Ile Pro Gln Leu Leu
          290         295         300
Ala Pro Asp Pro Arg Asp Gln Phe Gln His Thr Ala Arg Glu Ala Val
305         310         315         320
Ser Arg Arg Gly Ile Gly Leu Val Ser Thr Ser Asp Lys Val Asp Ala
          325         330         335
Asp Leu Leu Arg Arg Leu Ile Gly Asp Glu Ser Leu Arg Thr Ala Ala
          340         345         350
Arg Glu Val Arg Glu Glu Met Val Ala Leu Pro Thr Pro Ala Glu Thr
          355         360         365
Val Arg Arg Ile Val Glu Arg Ile Ser Gly
          370         375

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<210> 41  
 <211> 1035  
 <212> DNA

<213> Bacteria

<220>

<221> CDS

<222> (1)...(1035)

<400> 41

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1 5 10 15	
gag acc gtc acc gtc gag gaa gcc gtc gcc cag ggc ctg tac ccg cag	96
Glu Thr Val Thr Val Glu Glu Ala Val Ala Gln Gly Leu Tyr Pro Gln	
20 25 30	
gag gac atc gag acg cac ggg ctg ggc ggg gcc gcg atc gcc ggc gaa	144
Glu Asp Ile Glu Thr His Gly Leu Gly Gly Ala Ala Ile Ala Gly Glu	
35 40 45	
ctg ccc gcg ccg gac atg gcg ctg cgg gcc gcg cag gac gcc ctc aag	192
Leu Pro Ala Pro Asp Met Ala Leu Arg Ala Ala Gln Asp Ala Leu Lys	
50 55 60	
gag agc gag ctg ggc cgc ggc gac atc gac ctg ctg ctc tac gcg gcc	240
Glu Ser Glu Leu Gly Arg Gly Asp Ile Asp Leu Leu Leu Tyr Ala Ala	
65 70 75 80	
gcc tgg cac cag ggc ccc gag ggc tgg ctg gcg cac tcc tac atc cag	288
Ala Trp His Gln Gly Pro Glu Gly Trp Leu Ala His Ser Tyr Ile Gln	
85 90 95	
cac tac ctg ctc ggc ggg gtg ccc cgg gcg acc gag atc cgg cag ggc	336
His Tyr Leu Leu Gly Gly Val Pro Arg Ala Thr Glu Ile Arg Gln Gly	
100 105 110	
tgc aac ggc atg ttc acc atg ctc gaa ctc gcg gcc agc tac ctg aag	384
Cys Asn Gly Met Phe Thr Met Leu Glu Leu Ala Ala Ser Tyr Leu Lys	
115 120 125	
gcc gcg ccg gaa cgc aag gcg gcg atg ctc gtc gcc gcc gac aac tac	432
Ala Ala Pro Glu Arg Lys Ala Ala Met Leu Val Ala Ala Asp Asn Tyr	
130 135 140	
ggc acc ccg ctg ctg gac cgc tgg cgc acc aac ctc ggc ttc atc ctc	480
Gly Thr Pro Leu Leu Asp Arg Trp Arg Thr Asn Leu Gly Phe Ile Leu	
145 150 155 160	
ggc gac gcc gcc tcc gcg gtg gtg ctg agc acc gag agc ggc ttc gtc	528
Gly Asp Ala Ala Ser Ala Val Val Leu Ser Thr Glu Ser Gly Phe Val	
165 170 175	
gag ctg atg tgc gtc tgc tcc atc acc gtg ccg gag gcc gag gag gtg	576
Glu Leu Met Ser Val Cys Ser Ile Thr Val Pro Glu Ala Glu Glu Val	
180 185 190	
cac cgc ggc ggc gag ccg atg ttc ccg ccc ggc gcg acg ctc gcc aag	624
His Arg Gly Gly Glu Pro Met Phe Pro Pro Gly Ala Thr Leu Ala Lys	
195 200 205	



gag ctc gac ttc ggc gcc cgg ctc ttc tac cac atc acc gag cag acc	672
Glu Leu Asp Phe Gly Ala Arg Leu Phe Tyr His Ile Thr Glu Gln Thr	
210 215 220	
ccc gtg ctc gcc gtg ctc ggc gag gcg cag gag acg atg acc acc gtc	720
Pro Val Leu Ala Val Leu Gly Glu Ala Gln Glu Thr Met Thr Thr Val	
225 230 235 240	
gcc gag cag gcg ctc gcc gag gcc ggc atc ggc acg gga gac ctg gcc	768
Ala Glu Gln Ala Leu Ala Glu Ala Gly Ile Gly Thr Gly Asp Leu Ala	
245 250 255	
aag gtc tcc ttc atg aac tac tcc cgc gag gtg gtc gag cag cgc tgc	816
Lys Val Ser Phe Met Asn Tyr Ser Arg Glu Val Val Glu Gln Arg Cys	
260 265 270	
atg gcg ccc ctg ggg ctg ggg atg gag aag tcc acc tgg gac ttc ggg	864
Met Ala Pro Leu Gly Leu Gly Met Glu Lys Ser Thr Trp Asp Phe Gly	
275 280 285	
cgg atg atc ggg cac tgc ggc gcc agc gac cac ctg ctc gcc ctg cac	912
Arg Met Ile Gly His Cys Gly Ala Ser Asp His Leu Leu Ala Leu His	
290 295 300	
cac tcg ctg cgg gcc ggt gag gtc gcc gcc ggc gac cac gtg ctg tgg	960
His Ser Leu Arg Ala Gly Glu Val Ala Ala Gly Asp His Val Leu Trp	
305 310 315 320	
ctg gcg atg ggc ccc ggc gtg gag ttc acc gcc gcc gtc ctg cgc gta	1008
Leu Ala Met Gly Pro Gly Val Glu Phe Thr Ala Ala Val Leu Arg Val	
325 330 335	
ctg gac aac ccc tac gtc gag cgc tga	1035
Leu Asp Asn Pro Tyr Val Glu Arg *	
340	

<210> 42  
 <211> 344  
 <212> PRT  
 <213> Bacteria

<400> 42  
 Met Arg Thr Ala Gly Thr Tyr Ile Arg Gly Ile Gly Ala Tyr Leu Pro  
 1 5 10 15  
 Glu Thr Val Thr Val Glu Glu Ala Val Ala Gln Gly Leu Tyr Pro Gln  
 20 25 30  
 Glu Asp Ile Glu Thr His Gly Leu Gly Gly Ala Ala Ile Ala Gly Glu  
 35 40 45  
 Leu Pro Ala Pro Asp Met Ala Leu Arg Ala Ala Gln Asp Ala Leu Lys  
 50 55 60  
 Glu Ser Glu Leu Gly Arg Gly Asp Ile Asp Leu Leu Leu Tyr Ala Ala  
 65 70 75 80  
 Ala Trp His Gln Gly Pro Glu Gly Trp Leu Ala His Ser Tyr Ile Gln  
 85 90 95  
 His Tyr Leu Leu Gly Gly Val Pro Arg Ala Thr Glu Ile Arg Gln Gly  
 100 105 110

Cys Asn Gly Met Phe Thr Met Leu Glu Leu Ala Ala Ser Tyr Leu Lys  
 115 120 125  
 Ala Ala Pro Glu Arg Lys Ala Ala Met Leu Val Ala Ala Asp Asn Tyr  
 130 135 140  
 Gly Thr Pro Leu Leu Asp Arg Trp Arg Thr Asn Leu Gly Phe Ile Leu  
 145 150 155 160  
 Gly Asp Ala Ala Ser Ala Val Val Leu Ser Thr Glu Ser Gly Phe Val  
 165 170 175  
 Glu Leu Met Ser Val Cys Ser Ile Thr Val Pro Glu Ala Glu Glu Val  
 180 185 190  
 His Arg Gly Gly Glu Pro Met Phe Pro Pro Gly Ala Thr Leu Ala Lys  
 195 200 205  
 Glu Leu Asp Phe Gly Ala Arg Leu Phe Tyr His Ile Thr Glu Gln Thr  
 210 215 220  
 Pro Val Leu Ala Val Leu Gly Glu Ala Gln Glu Thr Met Thr Thr Val  
 225 230 235 240  
 Ala Glu Gln Ala Leu Ala Glu Ala Gly Ile Gly Thr Gly Asp Leu Ala  
 245 250 255  
 Lys Val Ser Phe Met Asn Tyr Ser Arg Glu Val Val Glu Gln Arg Cys  
 260 265 270  
 Met Ala Pro Leu Gly Leu Gly Met Glu Lys Ser Thr Trp Asp Phe Gly  
 275 280 285  
 Arg Met Ile Gly His Cys Gly Ala Ser Asp His Leu Leu Ala Leu His  
 290 295 300  
 His Ser Leu Arg Ala Gly Glu Val Ala Ala Gly Asp His Val Leu Trp  
 305 310 315 320  
 Leu Ala Met Gly Pro Gly Val Glu Phe Thr Ala Ala Val Leu Arg Val  
 325 330 335  
 Leu Asp Asn Pro Tyr Val Glu Arg  
 340

<210> 43  
 <211> 1347  
 <212> DNA  
 <213> .

<220>  
 <221> CDS  
 <222> (1)...(1347)

<400> 43  
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 Val Thr Gly Arg Asp Asp Arg Pro Asp Gly Ala Arg Pro Val Pro Pro  
 1 5 10 15  
 ggg cca gcg gtc acg ccc ggg cca gcg gtc acg ccc ggg ccg ccg gtc 96  
 Gly Pro Ala Val Thr Pro Gly Pro Ala Val Thr Pro Gly Pro Pro Val  
 20 25 30  
 acg cca ggg cgg gcg gcg gac gga ccg gcc gag gcc ggg agc gcg gcc 144  
 Thr Pro Gly Arg Ala Ala Asp Gly Pro Ala Glu Ala Gly Ser Ala Ala  
 35 40 45  
 ggg atc gac gcg ttt ccg ctg ccc cgc cgg tgc ccg ttc ggc ccg ccg 192  
 Gly Ile Asp Ala Phe Pro Leu Pro Arg Arg Cys Pro Phe Gly Pro Pro  
 50 55 60



290	295	300	
cat ccg gag cgg ctc gcc cgc ctg cgc gcc gag ccg gac cgg ttc ccc			960
His Pro Glu Arg Leu Ala Arg Leu Arg Ala Glu Pro Asp Arg Phe Pro			
305	310	315	320
gcc gcc gtc gag gag ctg ctg cgg tac ttc acc atc gtc gag gcg gcg			1008
Ala Ala Val Glu Glu Leu Leu Arg Tyr Phe Thr Ile Val Glu Ala Ala			
	325	330	335
acc gcg cgg acc gcg acc gcc gac gtg acg gtc ggt ggg gtc acc atc			1056
Thr Ala Arg Thr Ala Thr Ala Asp Val Thr Val Gly Gly Val Thr Ile			
	340	345	350
cgg gcc ggg gag ggg gtg gtg gcg ctg ggc cag gcc gcc aac cgg gac			1104
Arg Ala Gly Glu Gly Val Val Ala Leu Gly Gln Ala Ala Asn Arg Asp			
	355	360	365
ccg gcg gcg ttc gac cgg ccg gac gag ttc gac ccg gac cgc gac gcc			1152
Pro Ala Ala Phe Asp Arg Pro Asp Glu Phe Asp Pro Asp Arg Asp Ala			
	370	375	380
cgg cac cac ctc gcc ttc ggc tac gga cga cac atc tgc ccc ggc cag			1200
Arg His His Leu Ala Phe Gly Tyr Gly Arg His Ile Cys Pro Gly Gln			
	385	390	400
cac ctg gcc cgg ctg gaa ctg gac gtc gcg ctg agc cgg ctg gtc cgg			1248
His Leu Ala Arg Leu Glu Leu Asp Val Ala Leu Ser Arg Leu Val Arg			
	405	410	415
cgg ctg ccc ggg ctg cgg ttg acc gtg gac gtg gac gac ctg ccg ctc			1296
Arg Leu Pro Gly Leu Arg Leu Thr Val Asp Val Asp Asp Leu Pro Leu			
	420	425	430
aag gag gac ggc aac atc ttc ggc ctg cac gcg ctg ccg gtc gcc tgg			1344
Lys Glu Asp Gly Asn Ile Phe Gly Leu His Ala Leu Pro Val Ala Trp			
	435	440	445
tga			1347
*			

<210> 44  
 <211> 448  
 <212> PRT  
 <213> Bacteria

<400> 44  
 Val Thr Gly Arg Asp Asp Arg Pro Asp Gly Ala Arg Pro Val Pro Pro  
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 Gly Pro Ala Val Thr Pro Gly Pro Ala Val Thr Pro Gly Pro Pro Val  
 20 25 30  
 Thr Pro Gly Arg Ala Ala Asp Gly Pro Ala Glu Ala Gly Ser Ala Ala  
 35 40 45  
 Gly Ile Asp Ala Phe Pro Leu Pro Arg Arg Cys Pro Phe Gly Pro Pro  
 50 55 60  
 Ala Glu Tyr Ala Arg Leu Arg Thr Glu Arg Pro Val Ala Arg Leu Pro

65					70					75				80	
Met	Leu	Gly	Gly	Asn	Thr	Ala	Trp	Val	Val	Ser	Arg	Tyr	Ala	Asp	Val
				85					90					95	
Lys	Arg	Val	Leu	Ser	Asp	Pro	Arg	Met	Ser	Ala	Asp	Arg	Arg	Arg	Ala
			100					105					110		
Gly	Phe	Pro	Arg	Phe	Ala	Pro	Thr	Thr	Glu	Ser	Gln	Arg	Gln	Ala	Ser
			115				120					125			
Phe	Ala	Asn	Phe	Arg	Pro	Pro	Leu	Asn	Trp	Met	Asp	Pro	Pro	Glu	His
			130				135				140				
Thr	Ala	Ala	Arg	Arg	Gln	Ile	Val	Asp	Glu	Phe	Ala	Ala	Arg	Arg	Val
145					150				155					160	
Arg	Gln	Leu	Arg	Pro	Leu	Val	Glu	Arg	Val	Val	Asp	Glu	His	Leu	Asp
				165					170					175	
Ala	Met	Thr	Ala	Gly	Arg	Ser	Ser	Ala	Asp	Leu	Val	Pro	Ser	Phe	Ser
			180					185					190		
Tyr	Pro	Val	Pro	Ser	Arg	Val	Ile	Cys	Glu	Met	Leu	Gly	Val	Pro	Tyr
			195				200					205			
Gly	Glu	His	Ala	Phe	Phe	Glu	Arg	Arg	Ser	Thr	Arg	Met	Leu	Ser	Arg
			210				215				220				
Gly	Val	Pro	Ala	Asp	Glu	Arg	Ala	Arg	Cys	Ala	Arg	Glu	Ile	Arg	Glu
225					230				235					240	
Phe	Leu	Asp	Gly	Val	Val	Thr	Asp	Lys	Glu	Arg	His	Pro	Gly	Asp	Asp
			245					250					255		
Val	Leu	Ser	Arg	Leu	Leu	Ala	Ala	Gln	Arg	Ala	Ala	Gly	Glu	Pro	Asp
			260					265					270		
His	Glu	Ala	Val	Val	Ser	Met	Ala	Phe	Val	Leu	Leu	Val	Ala	Gly	His
			275				280					285			
Val	Thr	Thr	Ser	Asn	Met	Ile	Ser	Leu	Ser	Val	Leu	Ala	Leu	Leu	Thr
			290				295				300				
His	Pro	Glu	Arg	Leu	Ala	Arg	Leu	Arg	Ala	Glu	Pro	Asp	Arg	Phe	Pro
305					310					315				320	
Ala	Ala	Val	Glu	Glu	Leu	Leu	Arg	Tyr	Phe	Thr	Ile	Val	Glu	Ala	Ala
			325						330				335		
Thr	Ala	Arg	Thr	Ala	Thr	Ala	Asp	Val	Thr	Val	Gly	Gly	Val	Thr	Ile
			340					345				350			
Arg	Ala	Gly	Glu	Gly	Val	Val	Ala	Leu	Gly	Gln	Ala	Ala	Asn	Arg	Asp
			355				360				365				
Pro	Ala	Ala	Phe	Asp	Arg	Pro	Asp	Glu	Phe	Asp	Pro	Asp	Arg	Asp	Ala
			370				375				380				
Arg	His	His	Leu	Ala	Phe	Gly	Tyr	Gly	Arg	His	Ile	Cys	Pro	Gly	Gln
385					390				395					400	
His	Leu	Ala	Arg	Leu	Glu	Leu	Asp	Val	Ala	Leu	Ser	Arg	Leu	Val	Arg
			405					410					415		
Arg	Leu	Pro	Gly	Leu	Arg	Leu	Thr	Val	Asp	Val	Asp	Asp	Leu	Pro	Leu
			420					425				430			
Lys	Glu	Asp	Gly	Asn	Ile	Phe	Gly	Leu	His	Ala	Leu	Pro	Val	Ala	Trp
			435				440					445			

<210> 45  
 <211> 588  
 <212> DNA  
 <213> Bacteria  
  
 <220>  
 <221> CDS  
 <222> (1) ... (588)

<400> 45  
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 Arg Pro His Pro Trp Arg Pro Gly Arg Ser Arg Cys Ala Arg Cys Ala  
 1 5 10 15

act ggt acc gcg ccg acg acg aga tcc gcc acc gct ccg gcc ggt tct 96  
 Thr Gly Thr Ala Pro Thr Thr Arg Ser Ala Thr Ala Pro Ala Gly Ser  
 20 25 30

tcc gca tcg tcg gcc ggc ggg tgc ggg cca gca acc gcg agg tgt ccc 144  
 Ser Ala Ser Ser Ala Gly Gly Cys Gly Pro Ala Thr Ala Arg Cys Pro  
 35 40 45

agt ggt gcc agc cgt tgc tgg cac cgt gcg gga cgg gtc tgg tgg cgt 192  
 Ser Gly Ala Ser Arg Cys Trp His Arg Ala Gly Arg Val Trp Trp Arg  
 50 55 60

tcg tcg tcc gac gca tcg acg gcg tgc tgc acg tgc tcg ccc acg ccg 240  
 Ser Ser Ser Asp Ala Ser Thr Ala Cys Cys Thr Cys Ser Pro Thr Pro  
 65 70 75 80

acc tgc ggc ccg gct acc ggg aca ccg tcg agc tgg gac cga ccg tgc 288  
 Thr Cys Gly Pro Ala Thr Gly Thr Pro Ser Ser Trp Asp Arg Pro Cys  
 85 90 95

agt gca ccc ccg gac aac ttc acc ggc ccg gcc cgg gac ggc cgc ccg 336  
 Ser Ala Pro Arg Asp Asn Phe Thr Gly Pro Ala Arg Asp Gly Arg Pro  
 100 105 110

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 Val Leu Gln Ser Glu Glu Gly Gly Arg Phe His His Ala Val Thr Arg  
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 His Met Val Val Glu Val Gly Pro Asp Phe Pro Thr Ala Thr Pro Pro  
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 Asp Tyr Thr Trp Leu Thr Leu Arg Gln Leu Thr Ala Val Ala Ala Phe  
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agc tat cag gtc aac atc gag gcg cgc agc ctc ctg ctc tgc ctg ccg 576  
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 Ala Leu Arg \*  
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[illegible]

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His Ala Gly Leu Pro Pro Thr Arg Leu Ala Gly Thr Asp Thr Gly Val	
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Leu Pro Thr Val Glu Ala Tyr Thr Gly Ile Gly Ala Ala Thr Cys Ala	
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ctg gcc aac cgc atc tcc tac gcg ctg gac ctg cac ggc ccg agc gtc	528
Leu Ala Asn Arg Ile Ser Tyr Ala Leu Asp Leu His Gly Pro Ser Val	
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gcc gag gac acg gtc tgc tcg gcg tcg ctg gtc gcg gtg cac ctg gcc	576
Ala Glu Asp Thr Val Cys Ser Ala Ser Leu Val Ala Val His Leu Ala	
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His Ala Gly Leu Pro Pro Thr Arg Leu Ala Gly Thr Asp Thr Gly Val	
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130 135 140	



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 145 150 155 160  
 Leu Ala Asn Arg Ile Ser Tyr Ala Leu Asp Leu His Gly Pro Ser Val  
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 Cys Gln Ser Leu Leu  
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Gly Asp Gly Asp Thr Val Arg Phe Arg Leu Thr Met His Pro Asp Glu
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Thr Arg Gln Val Arg Ala Arg Arg Val Glu Thr Gly Pro Phe Glu Tyr
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Ala Gly Met Thr Asp Arg Ile Asn Ala Asn Ser Ala Val Gln Leu Ala
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Val Ile Arg Asp Lys Ile Glu Arg Leu Ala Arg Glu Gly Thr Ala Gly
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Val Gly Ser Thr Ser Gly Phe Met Gly Val Ala Thr Leu Arg Pro Gly
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gag cgg atc gcc gag cac tac cat ccc tac agc gag gag ttc ctg tac 192
Glu Arg Ile Ala Glu His Tyr His Pro Tyr Ser Glu Glu Phe Leu Tyr
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Val Ala Arg Gly Ala Ile Thr Ala Asp Leu Asp Asp Glu Pro Val Pro
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ccc ctc gcc ccc cgg ccc gaa ctc ggc cac gtc gac acc gag ctc gtc 384
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Glu Arg Ile Ala Glu His Tyr His Pro Tyr Ser Glu Glu Phe Leu Tyr
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Leu Arg Asn Thr Gly Asp Glu Pro Ala Glu Val Val Phe His Leu Gly
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 atg gcc ctg gag cag gag tac gtc acg gtc agc gac acc ggc cgc cgg 384  
 Met Ala Leu Glu Gln Glu Tyr Val Thr Val Ser Asp Thr Gly Arg Arg  
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 Trp Leu Val Asp Ala Ala Arg Gly Gly Pro Tyr Leu Tyr Gln Ala Leu  
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 ggc ccc gcg cag gtg gtc tcc acc ggc tgc acc tcg ggc atc gac gcc 528  
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<213> Bacteria

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Glu Arg Asp Arg Ala Gly Val Val Leu Gly Thr Ala Val Gly Gly Thr  
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Val Pro Ser Ser Leu Ala Ala Asp Val Ala Cys Arg His Gly Leu His  
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Gly Pro Ala Gln Val Val Ser Thr Gly Cys Thr Ser Gly Ile Asp Ala  
165 170 175  
Ile Gly Tyr Ala His Gln Leu Ile Ala Asp Gly Glu Ala Asp Ile Val  
180 185 190  
Leu Ala Gly Ala Ala Asp Ser Pro Ile Ser Pro Val Thr Val Ala Ser  
195 200 205  
Phe Asp Ala Ile Lys Ala Thr Ser Pro Asp Asn Asp Asp Pro Ala His  
210 215 220  
Ala Ser Arg Pro Phe Asp Ala Asp Arg His Gly Phe Val Leu Ala Glu  
225 230 235 240  
Gly Ala Ala Val Leu Val Leu Glu Glu Ala Gly His Ala Arg Arg Arg  
245 250 255  
Gly Ala His Val Tyr Cys Glu Val Ala Gly Tyr Ala Ser Arg Ser Asn  
260 265 270  
Gly Tyr His Met Thr Gly Leu Arg Pro Asp Gly Leu Glu Met Gly Leu  
275 280 285  
Ala Ile Ser Ala Ala Leu Lys Gln Gly Arg Ile Ala Pro Glu Gln Val  
290 295 300  
Ser Tyr Ile Ser Ala His Gly Ser Gly Thr Arg Gln Asn Asp Arg His  
305 310 315 320  
Glu Thr Ala Ala Phe Lys Arg Ala Leu Gly Gln Ala Ala Tyr Arg Val  
325 330 335  
Pro Ile Ser Ser Ile Lys Ser Met Val Gly His Ser Leu Gly Ala Ile  
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<211> 969

<212> DNA

<213> Bacteria

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tac ggg cac gcc gtc ggc gcc cgg ggc ccg gac gag gcc gtc ggg gcg	192
Tyr Gly His Ala Val Gly Ala Arg Gly Pro Asp Glu Ala Val Gly Ala	
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ctg gag acc gtc gcg ccg gac ctg cgc ggg ttc gcg tac gag ggc gcg	240
Leu Glu Thr Val Ala Pro Asp Leu Arg Gly Phe Ala Tyr Glu Gly Ala	
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gcg atg ggc ctc gcc gtc ctg gac ggg ctg acc ggt ggc cgc cgg atc	288
Ala Met Gly Leu Ala Val Leu Asp Gly Leu Thr Gly Gly Arg Arg Ile	
85 90 95	
gcc cgg ttc ctg gcc ggg ccg gcc gcc cgg cac gtg tac atg gtc cat	336
Ala Arg Phe Leu Ala Gly Pro Ala Ala Arg His Val Tyr Met Val His	
100 105 110	
gtc ggg gtg ggc tgg gcg atg gcc cgc ctg ccc cgc tgg cgt cgg cac	384
Val Gly Val Gly Trp Ala Met Ala Arg Leu Pro Arg Trp Arg Arg His	
115 120 125	
gcg atc caa ccc gcc gac cgg ctg ctg ggc tgg ctg gcg ctg gac ggc	432
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Tyr Gly Phe His Gln Ala Tyr Phe His Thr Arg Arg Tyr Val Trp Ser	
145 150 155 160	
cac cgg cgt gac gag gtg ctg ccc tgg ccc ggc gac ccg atc ggg cgg	528
His Arg Arg Asp Glu Val Leu Pro Trp Pro Gly Asp Pro Ile Gly Arg	
165 170 175	
tgg acc ggg cgc gtc gtg gac cag ggc atc ggc cgc gcg ctg tgg ttc	576
Trp Thr Gly Arg Val Val Asp Gln Gly Ile Gly Arg Ala Leu Trp Phe	
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gtc gag ggc gcc gac acc gac cgg atc gcc gac acc gtc gac ggc ttc	624
Val Glu Gly Ala Asp Thr Asp Arg Ile Ala Asp Thr Val Asp Gly Phe	
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Ala	Thr	Asp	Val	Phe	Cys	Gly	Ala	Pro	Pro	Ala	Glu	Ala	Ala	Ala	Val		
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Thr	Gln	Ala	Ala	Leu	Ala	Asp	Leu	Asp	Arg	Asp	Gly	Pro	Glu	Pro	Ala		
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Tyr	Leu	Val	Trp	Arg	Gln	Arg	Ile	Ala	Lys	Gln	Phe	Val	Thr	Leu	Gly		
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agg	tgc	tga														969	
Arg	Cys	*															

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 <213> Bacteria

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 165 170 175  
 Trp Thr Gly Arg Val Val Asp Gln Gly Ile Gly Arg Ala Leu Trp Phe  
 180 185 190  
 Val Glu Gly Ala Asp Thr Asp Arg Ile Ala Asp Thr Val Asp Gly Phe  
 195 200 205  
 Pro Pro Asp Arg His Glu Asp Leu Tyr Ser Gly Val Ala Leu Ala Ala  
 210 215 220  
 Thr Tyr Ala Gly Gly Ala Pro Pro Glu Asp Leu Arg Arg Leu Arg Glu  
 225 230 235 240  
 Arg Gly Gly Ala Tyr Ala Pro Ala Met Ala Gln Gly Ser Ala Phe Ala  
 245 250 255  
 Ala Glu Ala Arg Glu Arg Ala Gly Leu Thr Thr Ala His Thr Ala Val  
 260 265 270  
 Ala Thr Asp Val Phe Cys Gly Ala Pro Pro Ala Glu Ala Ala Val  
 275 280 285  
 Thr Gln Ala Ala Leu Ala Asp Leu Asp Arg Asp Gly Pro Glu Pro Ala  
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<211> 1956

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<213> Bacteria

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Gly Met Tyr Val Leu Val Arg Gln Pro Glu Ala Asn Ala Asp Glu Arg	
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cgc gcc atg gcg gag ccg tac cgg ttc acg ccg atg tcg ctg ccg atg	144
Arg Ala Met Ala Glu Pro Tyr Arg Phe Thr Pro Met Ser Leu Pro Met	
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ccg ggc ggc ctg ccg cag cag tcg atc cgc cgg gtc aac ggc gcg tac	192
Pro Gly Gly Leu Pro Gln Gln Ser Ile Arg Arg Val Asn Gly Ala Tyr	
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cag cac ctg gcg gcg tgg atc tcc tcc gtc ggc gcc ggc gcc gcg atg	240
Gln His Leu Ala Ala Trp Ile Ser Ser Val Gly Ala Gly Ala Ala Met	
65 70 75 80	
aac gac ctg gac ggt gac gga ctg gcc aac gac ctg tgc gtc acc gac	288
Asn Asp Leu Asp Gly Asp Gly Leu Ala Asn Asp Leu Cys Val Thr Asp	
85 90 95	

cca cgc gtc gac cgc gtc gtg gtg acc ccg gcc ccg acc gcc ggc gcc	336
Pro Arg Val Asp Arg Val Val Val Thr Pro Ala Pro Thr Ala Gly Ala	
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gac cgc tac cag ccg ttc gtg ctg gac ccg gcg ccg ctg ccg atg aac	384
Asp Arg Tyr Gln Pro Phe Val Leu Asp Pro Ala Pro Leu Pro Met Asn	
115 120 125	
ccg tac gtc gcc ccg atg ggc tgc ctg ccc ggc gac ctc aac gcc gac	432
Pro Tyr Val Ala Pro Met Gly Cys Leu Pro Gly Asp Leu Asn Ala Asp	
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ggc cgc acc gac ctg ctc gtg tac tgg tgg ggc cgg acc ccg gtg gtc	480
Gly Arg Thr Asp Leu Leu Val Tyr Trp Trp Gly Arg Thr Pro Val Val	
145 150 155 160	
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Phe Leu Ala Arg Ala Asp Ala Thr Gly Leu Ser Arg Ala Ala Tyr His	
165 170 175	
ccc gtc gag ctg gtg ccg ggc gcg gcg acc ggc ggt agc cgg tac gac	576
Pro Val Glu Leu Val Pro Gly Ala Ala Thr Gly Gly Ser Arg Tyr Asp	
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225 230 235 240	
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Gly Thr Ala Gly Ala Thr Pro Ser Ala Ser Phe Ala Glu Val Pro Asp	
260 265 270	
gtc ttc gac acc aag gtc tcc ccg ggc tgg acg ctc gcc gtc gcc gcg	864
Val Phe Asp Thr Lys Val Ser Arg Gly Trp Thr Leu Ala Val Ala Ala	
275 280 285	
aac gac ctc gac ggc gac caa ctg ccc gag ctg tac gtg gcc aac gac	912
Asn Asp Leu Asp Gly Asp Gln Leu Pro Glu Leu Tyr Val Ala Asn Asp	
290 295 300	
ttc ggg ccg gac ccg ctg ctg cac aac ccg tcc gag ccg ggc ccg atc	960
Phe Gly Pro Asp Arg Leu Leu His Asn Arg Ser Glu Arg Gly Arg Ile	
305 310 315 320	
gcc ttc gcg ccg gtc gag agc ccc ggc ctg ccc ggc ctg acc ccc aag	1008
Ala Phe Ala Pro Val Glu Ser Pro Gly Leu Pro Gly Leu Thr Pro Lys	

	325	330	335	
tca aag cgg ctc ggc cac gac tcg ttc aag ggc atg ggc gtg gac ttc				1056
Ser Lys Arg Leu Gly His Asp Ser Phe Lys Gly Met Gly Val Asp Phe				
	340	345	350	
ggc gac atc gac ggc gac ggc atg ttc gac ctg tac gtc ggc aac atc				1104
Gly Asp Ile Asp Gly Asp Gly Met Phe Asp Leu Tyr Val Gly Asn Ile				
	355	360	365	
acc acc tcc ttc ggc atc cag gag agc aac ttc gcc ttc gtc aac acc				1152
Thr Thr Ser Phe Gly Ile Gln Glu Ser Asn Phe Ala Phe Val Asn Thr				
	370	375	380	
gcc gcc gac acc gcc gcg ctg cgc gcc gcg ctg tgg gcc ggc gag gcg				1200
Ala Ala Asp Thr Ala Ala Leu Arg Ala Ala Leu Trp Ala Gly Glu Ala				
	385	390	395	400
ccg tgg cac gac cgc agc gcc gag ctg ggc ctg gcc tgg agc ggg tgg				1248
Pro Trp His Asp Arg Ser Ala Glu Leu Gly Leu Ala Trp Ser Gly Trp				
	405	410	415	
agc tgg gac gtc aag ttc ggc gac ttc acc aac cgc ggc gac ccg gcg				1296
Ser Trp Asp Val Lys Phe Gly Asp Phe Thr Asn Arg Gly Asp Pro Ala				
	420	425	430	
atc gtg cag acc tcc ggc ttc gtc aag ggc gag gtc aac cgc tgg gcg				1344
Ile Val Gln Thr Ser Gly Phe Val Lys Gly Glu Val Asn Arg Trp Ala				
	435	440	445	
cag ttg cag gag gcg gcc acc gcc aac gac gac ctg ctc gcc aac ccc				1392
Gln Leu Gln Glu Ala Ala Thr Ala Asn Asp Asp Leu Leu Ala Asn Pro				
	450	455	460	
cgc tgg tgg ccg aag gtc gag cag ggc gac gac atc gcc ggc ggc cag				1440
Arg Trp Trp Pro Lys Val Glu Gln Gly Asp Asp Ile Ala Gly Gly Gln				
	465	470	475	480
cac ctc gcc ttc cac gtc cgg ggc gcc gac ggc cgc tac gag gac ctc				1488
His Leu Ala Phe His Val Arg Gly Ala Asp Gly Arg Tyr Glu Asp Leu				
	485	490	495	
agc cac gaa ctg ggc ctg gcc gac cgg gtg ccc agc cgg ggc atc gcc				1536
Ser His Glu Leu Gly Leu Ala Asp Arg Val Pro Ser Arg Gly Ile Ala				
	500	505	510	
acc gcc gac gcc gac ggc gac ggg cgc ctc gac ctc gtc gtc gcc cgg				1584
Thr Ala Asp Ala Asp Gly Asp Gly Arg Leu Asp Leu Val Val Ala Arg				
	515	520	525	
cag tgg gac gcg ccg gtc ttc tac cgc aac gac agc ccg gac acc ggt				1632
Gln Trp Asp Ala Pro Val Phe Tyr Arg Asn Asp Ser Pro Asp Thr Gly				
	530	535	540	
tcc ttc ctc acc ctg cgg ctg ctg cac gag cag gcg ccg gcc gcc ggc				1680
Ser Phe Leu Thr Leu Arg Leu Leu His Glu Gln Ala Pro Ala Ala Gly				
	545	550	555	560

ccc ctc gcc ggg gcg ggg tcg ccg gtc gtc ggc gcg cag gtc cgg gtg	1728
Pro Leu Ala Gly Ala Gly Ser Pro Val Val Gly Ala Gln Val Arg Val	
565 570 575	

acc acg ccg gac ggc ccg gtg ctc atc gac ccg gtc gac ggc ggc agc	1776
Thr Thr Pro Asp Gly Arg Val Leu Ile Asp Arg Val Asp Gly Gly Ser	
580 585 590	

ggc cac tcg ggc ccg cgc agc aac gag gtg tcg ctc ggt ctc gac gac	1824
Gly His Ser Gly Arg Arg Ser Asn Glu Val Ser Leu Gly Leu Asp Asp	
595 600 605	

gtg acc ggc ccg gtg tcg gtc cac ctc acc tgg ccg gac ccg tcc ggc	1872
Val Thr Gly Pro Val Ser Val His Leu Thr Trp Arg Asp Arg Ser Gly	
610 615 620	

gcc ccg cac gag cag gag ctg acg ctg gcc ccc ggt cga cac acc ctc	1920
Ala Pro His Glu Gln Glu Leu Thr Leu Ala Pro Gly Arg His Thr Leu	
625 630 635 640	

acc ctc ggt tcg cag gct ccg gag gtc tcg cga tga	1956
Thr Leu Gly Ser Gln Ala Arg Glu Val Ser Arg *	
645 650	

<210> 58  
 <211> 651  
 <212> PRT  
 <213> Bacteria

<400> 58	
Met Phe Arg Arg Gln Leu Ala Gly Leu Val Ala Leu Val Leu Leu Thr	
1 5 10 15	
Gly Met Tyr Val Leu Val Arg Gln Pro Glu Ala Asn Ala Asp Glu Arg	
20 25 30	
Arg Ala Met Ala Glu Pro Tyr Arg Phe Thr Pro Met Ser Leu Pro Met	
35 40 45	
Pro Gly Gly Leu Pro Gln Gln Ser Ile Arg Arg Val Asn Gly Ala Tyr	
50 55 60	
Gln His Leu Ala Ala Trp Ile Ser Ser Val Gly Ala Gly Ala Ala Met	
65 70 75 80	
Asn Asp Leu Asp Gly Asp Gly Leu Ala Asn Asp Leu Cys Val Thr Asp	
85 90 95	
Pro Arg Val Asp Arg Val Val Val Thr Pro Ala Pro Thr Ala Gly Ala	
100 105 110	
Asp Arg Tyr Gln Pro Phe Val Leu Asp Pro Ala Pro Leu Pro Met Asn	
115 120 125	
Pro Tyr Val Ala Pro Met Gly Cys Leu Pro Gly Asp Leu Asn Ala Asp	
130 135 140	
Gly Arg Thr Asp Leu Leu Val Tyr Trp Trp Gly Arg Thr Pro Val Val	
145 150 155 160	
Phe Leu Ala Arg Ala Asp Ala Thr Gly Leu Ser Arg Ala Ala Tyr His	
165 170 175	
Pro Val Glu Leu Val Pro Gly Ala Ala Thr Gly Gly Ser Arg Tyr Asp	
180 185 190	
Gly Pro Lys Trp Asn Thr Asn Ala Ala Thr Leu Ala Asp Phe Asp Gly	
195 200 205	
Asp Gly His Leu Asp Val Tyr Ile Gly Asn Tyr Phe Pro Asp Ser Ala	

210	215	220
Val Leu Asp Asp Thr	Val His Gly Gly	Val Ala Met Asn Arg Ser Met
225	230	235
Ser Asn Gly Leu Asn Gly Gly Glu Asp His Val Phe Arg Trp Thr Gly		240
	245	250
Gly Thr Ala Gly Ala Thr Pro Ser Ala Ser Phe Ala Glu Val Pro Asp		255
	260	265
Val Phe Asp Thr Lys Val Ser Arg Gly Trp Thr Leu Ala Val Ala Ala		270
	275	280
Asn Asp Leu Asp Gly Asp Gln Leu Pro Glu Leu Tyr Val Ala Asn Asp		285
	290	295
Phe Gly Pro Asp Arg Leu Leu His Asn Arg Ser Glu Arg Gly Arg Ile		300
305	310	315
Ala Phe Ala Pro Val Glu Ser Pro Gly Leu Pro Gly Leu Thr Pro Lys		320
	325	330
Ser Lys Arg Leu Gly His Asp Ser Phe Lys Gly Met Gly Val Asp Phe		335
	340	345
Gly Asp Ile Asp Gly Asp Gly Met Phe Asp Leu Tyr Val Gly Asn Ile		350
	355	360
Thr Thr Ser Phe Gly Ile Gln Glu Ser Asn Phe Ala Phe Val Asn Thr		365
	370	375
Ala Ala Asp Thr Ala Ala Leu Arg Ala Ala Leu Trp Ala Gly Glu Ala		380
385	390	395
Pro Trp His Asp Arg Ser Ala Glu Leu Gly Leu Ala Trp Ser Gly Trp		400
	405	410
Ser Trp Asp Val Lys Phe Gly Asp Phe Thr Asn Arg Gly Asp Pro Ala		415
	420	425
Ile Val Gln Thr Ser Gly Phe Val Lys Gly Glu Val Asn Arg Trp Ala		430
	435	440
Gln Leu Gln Glu Ala Ala Thr Ala Asn Asp Asp Leu Leu Ala Asn Pro		445
	450	455
Arg Trp Trp Pro Lys Val Glu Gln Gly Asp Asp Ile Ala Gly Gly Gln		460
465	470	475
His Leu Ala Phe His Val Arg Gly Ala Asp Gly Arg Tyr Glu Asp Leu		480
	485	490
Ser His Glu Leu Gly Leu Ala Asp Arg Val Pro Ser Arg Gly Ile Ala		495
	500	505
Thr Ala Asp Ala Asp Gly Asp Gly Arg Leu Asp Leu Val Val Ala Arg		510
	515	520
Gln Trp Asp Ala Pro Val Phe Tyr Arg Asn Asp Ser Pro Asp Thr Gly		525
	530	535
Ser Phe Leu Thr Leu Arg Leu Leu His Glu Gln Ala Pro Ala Ala Gly		540
545	550	555
Pro Leu Ala Gly Ala Gly Ser Pro Val Val Gly Ala Gln Val Arg Val		560
	565	570
Thr Thr Pro Asp Gly Arg Val Leu Ile Asp Arg Val Asp Gly Gly Ser		575
	580	585
Gly His Ser Gly Arg Arg Ser Asn Glu Val Ser Leu Gly Leu Asp Asp		590
	595	600
Val Thr Gly Pro Val Ser Val His Leu Thr Trp Arg Asp Arg Ser Gly		605
	610	615
Ala Pro His Glu Gln Glu Leu Thr Leu Ala Pro Gly Arg His Thr Leu		620
625	630	635
Thr Leu Gly Ser Gln Ala Arg Glu Val Ser Arg		640
	645	650

<210> 59

<211> 630  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(630)

<400> 59

atg ggc gaa acg gga cgt cag ttg gcc gtc gtc acg gcg gac gcc gac	48
Met Gly Glu Thr Gly Arg Gln Leu Ala Val Val Thr Ala Asp Ala Asp	
1 5 10 15	
gtc gtg gag gcg gag ctg gtg gac gac gag acg gcc ggc gcc tcc gtc	96
Val Val Glu Ala Glu Leu Val Asp Asp Glu Thr Ala Gly Ala Ser Val	
20 25 30	
gtc gtc cac acg gac cgc gac cgg cac ctc tcc ccc gag acc gtc gcc	144
Val Val His Thr Asp Arg Asp Arg His Leu Ser Pro Glu Thr Val Ala	
35 40 45	
gcc atc gcg gcg agc gtc gcc gac tcc acc cgc cgc gcg tac ggc acc	192
Ala Ile Ala Ala Ser Val Ala Asp Ser Thr Arg Arg Ala Tyr Gly Thr	
50 55 60	
gac cgg gcc gcg ttc gcc gcc tgg tgc gcc gag gag gac cgc acg gcc	240
Asp Arg Ala Ala Phe Ala Ala Trp Cys Ala Glu Glu Asp Arg Thr Ala	
65 70 75 80	
gtc ccc gcg tcg gcg gag acg atg gcg gag tgg gtg cgg cac ctg acc	288
Val Pro Ala Ser Ala Glu Thr Met Ala Glu Trp Val Arg His Leu Thr	
85 90 95	
gtc acg ccc cgc ccc cgg acg cag cga ccg gcc ggg ccg tcg acc atc	336
Val Thr Pro Arg Pro Arg Thr Gln Arg Pro Ala Gly Pro Ser Thr Ile	
100 105 110	
gag cgg gcc atg tcc gcc gtg acc acc tgg cac gag gag cag gga cgg	384
Glu Arg Ala Met Ser Ala Val Thr Thr Trp His Glu Glu Gln Gly Arg	
115 120 125	
ccg aag ccg aac atg cgc ggc gcc cgg gcc gtc ctc aac gcc tac aag	432
Pro Lys Pro Asn Met Arg Gly Ala Arg Ala Val Leu Asn Ala Tyr Lys	
130 135 140	
gac cgg ctc gcc gtg gag aag gcg gag gcc gcg cag gcc cgc cag gcg	480
Asp Arg Leu Ala Val Glu Lys Ala Glu Ala Ala Gln Ala Arg Gln Ala	
145 150 155 160	
acc gcc gcc ctc ccc ccg cag atc cgc gcc atg ctc gcc ggg gtc gac	528
Thr Ala Ala Leu Pro Pro Gln Ile Arg Ala Met Leu Ala Gly Val Asp	
165 170 175	
cgg acc acc ctc gcc ggg aag cgg aac gcg gcc tgg tcc tcc tcg gtt	576
Arg Thr Thr Leu Ala Gly Lys Arg Asn Ala Ala Trp Ser Ser Ser Val	
180 185 190	
cgc cac ggc ggc cgc gtc ctc cga gct ggt cgc agc tgg acg tcg aca	624

Arg His Gly Gly Arg Val Leu Arg Ala Gly Arg Ser Trp Thr Ser Thr  
 195 200 205

cgg tga  
 Arg \*

630

<210> 60  
 <211> 209  
 <212> PRT  
 <213> Bacteria

<400> 60  
 Met Gly Glu Thr Gly Arg Gln Leu Ala Val Val Thr Ala Asp Ala Asp  
 1 5 10 15  
 Val Val Glu Ala Glu Leu Val Asp Asp Glu Thr Ala Gly Ala Ser Val  
 20 25 30  
 Val Val His Thr Asp Arg Asp Arg His Leu Ser Pro Glu Thr Val Ala  
 35 40 45  
 Ala Ile Ala Ala Ser Val Ala Asp Ser Thr Arg Arg Ala Tyr Gly Thr  
 50 55 60  
 Asp Arg Ala Ala Phe Ala Ala Trp Cys Ala Glu Glu Asp Arg Thr Ala  
 65 70 75 80  
 Val Pro Ala Ser Ala Glu Thr Met Ala Glu Trp Val Arg His Leu Thr  
 85 90 95  
 Val Thr Pro Arg Pro Arg Thr Gln Arg Pro Ala Gly Pro Ser Thr Ile  
 100 105 110  
 Glu Arg Ala Met Ser Ala Val Thr Thr Trp His Glu Glu Gln Gly Arg  
 115 120 125  
 Pro Lys Pro Asn Met Arg Gly Ala Arg Ala Val Leu Asn Ala Tyr Lys  
 130 135 140  
 Asp Arg Leu Ala Val Glu Lys Ala Glu Ala Ala Gln Ala Arg Gln Ala  
 145 150 155 160  
 Thr Ala Ala Leu Pro Pro Gln Ile Arg Ala Met Leu Ala Gly Val Asp  
 165 170 175  
 Arg Thr Thr Leu Ala Gly Lys Arg Asn Ala Ala Trp Ser Ser Ser Val  
 180 185 190  
 Arg His Gly Gly Arg Val Leu Arg Ala Gly Arg Ser Trp Thr Ser Thr  
 195 200 205  
 Arg

<210> 61  
 <211> 1566  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(1566)

<400> 61  
 gtg ttc ttc gag gac tgc acc ctc gcg gag gcc acc tat ccc acg ctg 48  
 Val Phe Phe Glu Asp Cys Thr Leu Ala Glu Ala Thr Tyr Pro Thr Leu  
 1 5 10 15

ttc gcc ggg gtg gac gtc gtg ccg tcc agc gtc gac ctc cag cgc gtg	96
Phe Ala Gly Val Asp Val Val Pro Ser Ser Val Asp Leu Gln Arg Val	
20 25 30	
gag tac gaa cgg ccc atc ggc gcg gag cag ggc ctc gcc gcc gcc ctg	144
Glu Tyr Glu Arg Pro Ile Gly Ala Glu Gln Gly Leu Ala Ala Ala Leu	
35 40 45	
gcg cag gag gcg gag gag gcc ggc ggc cgc tcc ccg tac gac gtg acc	192
Ala Gln Glu Ala Glu Glu Ala Gly Gly Arg Ser Pro Tyr Asp Val Thr	
50 55 60	
ctg atc gac gcc gcg ccg tcc ctc ggg ctg gtc acc gtt gcc gca ctc	240
Leu Ile Asp Ala Ala Pro Ser Leu Gly Leu Val Thr Val Ala Ala Leu	
65 70 75 80	
acc gcc gcc gac gag gcc ctg gtg ccc atc aag gtc ggc ggc ctg gac	288
Thr Ala Ala Asp Glu Ala Leu Val Pro Ile Lys Val Gly Gly Leu Asp	
85 90 95	
atg aag gcc atg gcg tcc ctc cac aag acg ctc cgc agc gtc cag cgg	336
Met Lys Ala Met Ala Ser Leu His Lys Thr Leu Arg Ser Val Gln Arg	
100 105 110	
aag acg aac ccg aag ctg agc gtc ggg gcc gtc ctg ctg acc gcg tgg	384
Lys Thr Asn Pro Lys Leu Ser Val Gly Ala Val Leu Leu Thr Ala Trp	
115 120 125	
gac aag agc acg ttt gcc ccg cag ctc gcc acg aag gtg agc gag gac	432
Asp Lys Ser Thr Phe Ala Arg Gln Leu Ala Thr Lys Val Ser Glu Asp	
130 135 140	
tac ccg gag gcg gcc gtc gtg ccg atc ccg cgc agc atc cgc gcg tcg	480
Tyr Pro Glu Ala Ala Val Val Pro Ile Arg Arg Ser Ile Arg Ala Ser	
145 150 155 160	
gag gcc ccg ctc tcc gag gag ccg atc cgc ctg tac gcg ccc gag gcg	528
Glu Ala Pro Leu Ser Glu Glu Pro Ile Arg Leu Tyr Ala Pro Glu Ala	
165 170 175	
gcc ccg gcc ggg gac tac gac cag tgc ggc cgc cgt cct cct gcc ggg	576
Ala Pro Ala Gly Asp Tyr Asp Gln Cys Gly Arg Arg Pro Pro Ala Gly	
180 185 190	
gag ggc tgc cgc gtg agc cgc cgc tcc ctc gcc ctc ccg tcg acc agg	624
Glu Gly Cys Arg Val Ser Arg Arg Ser Leu Ala Leu Pro Ser Thr Arg	
195 200 205	
agc acc gag ccg gac cac gcc gac gag ctg gag gcc gcc ccc gaa gag	672
Ser Thr Glu Pro Asp His Ala Asp Glu Leu Glu Ala Ala Pro Glu Glu	
210 215 220	
aag ctc gcg gcc gcg ccg tcc gcc ggg gtg gtc gcc tcg ctg acc ggc	720
Lys Leu Ala Ala Ala Arg Ser Ala Gly Val Val Ala Ser Leu Thr Gly	
225 230 235 240	
gcg gac ctg tcg acg ccc ctc acc gtg gcg cag ctc ccc acg ccg tac	768
Ala Asp Leu Ser Thr Pro Leu Thr Val Ala Gln Leu Pro Thr Pro Tyr	



	245	250	255	
	gac gtc gcg gag acc gtc acg gcg ccg ctg aac gac cag gag cgc ggt			816
	Asp Val Ala Glu Thr Val Thr Ala Pro Leu Asn Asp Gln Glu Arg Gly			
	260	265	270	
	tac ctg gac gtg tgc gag cag gcc ctc cac ggc ttc cgg aag tcc gtc			864
	Tyr Leu Asp Val Cys Glu Gln Ala Leu His Gly Phe Arg Lys Ser Val			
	275	280	285	
	gtc gtc gcg ggc aag gcc ctg gag gtc atc aac cgc ggc cgc ctc tac			912
	Val Val Ala Gly Lys Ala Leu Glu Val Ile Asn Arg Gly Arg Leu Tyr			
	290	295	300	
	cgg gag acg cac gag acg ttc gcg gac tac gtg acg gag gtg tgg gac			960
	Arg Glu Thr His Glu Thr Phe Ala Asp Tyr Val Thr Glu Val Trp Asp			
	305	310	315	320
	atg aag cgg gcc cac gcc tat cgg atg atc gag ggg tgg cga ccg gcc			1008
	Met Lys Arg Ala His Ala Tyr Arg Met Ile Glu Gly Trp Arg Pro Ala			
	325	330	335	
	gac ctc gtg tct cca att gga gac atc aac gag ggc cag gcc cgc gag			1056
	Asp Leu Val Ser Pro Ile Gly Asp Ile Asn Glu Gly Gln Ala Arg Glu			
	340	345	350	
	ctg gcg ccc gtg ctc aag gag tac ggg ccc gag gtg acc gtc acc ctg			1104
	Leu Ala Pro Val Leu Lys Glu Tyr Gly Pro Glu Val Thr Val Thr Leu			
	355	360	365	
	tac cgg ggg gtc aag gag ctg cgc ggc gac cgg cgg gtg acg gct gcg			1152
	Tyr Arg Gly Val Lys Glu Leu Arg Gly Asp Arg Arg Val Thr Ala Ala			
	370	375	380	
	gac ctc tcg gag gcc cgg gca gcg ctg cct ccg ccg aag cac ctc gcc			1200
	Asp Leu Ser Glu Ala Arg Ala Ala Leu Pro Pro Pro Lys His Leu Ala			
	385	390	395	400
	cgg ccg gac cag gtg cgc gac gtc ctc acc gtg gcg gcc gcc gag ggc			1248
	Arg Pro Asp Gln Val Arg Asp Val Leu Thr Val Ala Ala Ala Glu Gly			
	405	410	415	
	cgc gcg ccc cgg ctc gcc ccg gcc gag ccg aag gtg ccg gcc cag gcc			1296
	Arg Ala Pro Arg Leu Ala Pro Ala Glu Pro Lys Val Pro Ala Gln Ala			
	420	425	430	
	gcc gac gag cac cag gcc gag cag gtc gac gag ggc ggc gta agt cag			1344
	Ala Asp Glu His Gln Ala Glu Gln Val Asp Glu Gly Gly Val Ser Gln			
	435	440	445	
	gac cag gtc gac gag ggc gcg gag gcc atc gcc acc ctg gag gcc gcc			1392
	Asp Gln Val Asp Glu Gly Ala Glu Ala Ile Ala Thr Leu Glu Ala Ala			
	450	455	460	
	gtg gcc cag caa cgg cag atc tat gac cgg gtg ggc ggc ggg act ctc			1440
	Val Ala Gln Gln Arg Gln Ile Tyr Asp Arg Val Gly Gly Gly Thr Leu			
	465	470	475	480

gcg gcc gcc ctg ctg tac gac cca ggc cgg ggt gac cat ctg cgc cgc 1488  
 Ala Ala Ala Leu Leu Tyr Asp Pro Gly Arg Gly Asp His Leu Arg Arg  
                     485                    490                    495

gag ctg cgg cag tac gcg cag cgg acg gcg tac cgg gca cgg gat acc 1536  
 Glu Leu Arg Gln Tyr Ala Gln Arg Thr Ala Tyr Arg Ala Arg Asp Thr  
                     500                    505                    510

tcc ggt gag cag gtg gcc gac gac gcg taa 1566  
 Ser Gly Glu Gln Val Ala Asp Asp Ala \*  
                     515                    520

<210> 62  
 <211> 521  
 <212> PRT  
 <213> Bacteria

<400> 62  
 Val Phe Phe Glu Asp Cys Thr Leu Ala Glu Ala Thr Tyr Pro Thr Leu  
   1                    5                    10                    15  
 Phe Ala Gly Val Asp Val Val Pro Ser Ser Val Asp Leu Gln Arg Val  
                     20                    25                    30  
 Glu Tyr Glu Arg Pro Ile Gly Ala Glu Gln Gly Leu Ala Ala Ala Leu  
                     35                    40                    45  
 Ala Gln Glu Ala Glu Glu Ala Gly Gly Arg Ser Pro Tyr Asp Val Thr  
                     50                    55                    60  
 Leu Ile Asp Ala Ala Pro Ser Leu Gly Leu Val Thr Val Ala Ala Leu  
   65                    70                    75                    80  
 Thr Ala Ala Asp Glu Ala Leu Val Pro Ile Lys Val Gly Gly Leu Asp  
                     85                    90                    95  
 Met Lys Ala Met Ala Ser Leu His Lys Thr Leu Arg Ser Val Gln Arg  
                     100                    105                    110  
 Lys Thr Asn Pro Lys Leu Ser Val Gly Ala Val Leu Leu Thr Ala Trp  
                     115                    120                    125  
 Asp Lys Ser Thr Phe Ala Arg Gln Leu Ala Thr Lys Val Ser Glu Asp  
                     130                    135                    140  
 Tyr Pro Glu Ala Ala Val Val Pro Ile Arg Arg Ser Ile Arg Ala Ser  
   145                    150                    155                    160  
 Glu Ala Pro Leu Ser Glu Glu Pro Ile Arg Leu Tyr Ala Pro Glu Ala  
                     165                    170                    175  
 Ala Pro Ala Gly Asp Tyr Asp Gln Cys Gly Arg Arg Pro Pro Ala Gly  
                     180                    185                    190  
 Glu Gly Cys Arg Val Ser Arg Arg Ser Leu Ala Leu Pro Ser Thr Arg  
                     195                    200                    205  
 Ser Thr Glu Pro Asp His Ala Asp Glu Leu Glu Ala Ala Pro Glu Glu  
                     210                    215                    220  
 Lys Leu Ala Ala Ala Arg Ser Ala Gly Val Val Ala Ser Leu Thr Gly  
   225                    230                    235                    240  
 Ala Asp Leu Ser Thr Pro Leu Thr Val Ala Gln Leu Pro Thr Pro Tyr  
                     245                    250                    255  
 Asp Val Ala Glu Thr Val Thr Ala Pro Leu Asn Asp Gln Glu Arg Gly  
                     260                    265                    270  
 Tyr Leu Asp Val Cys Glu Gln Ala Leu His Gly Phe Arg Lys Ser Val  
                     275                    280                    285  
 Val Val Ala Gly Lys Ala Leu Glu Val Ile Asn Arg Gly Arg Leu Tyr  
                     290                    295                    300  
 Arg Glu Thr His Glu Thr Phe Ala Asp Tyr Val Thr Glu Val Trp Asp

305		310		315		320
Met Lys Arg Ala His	Ala Tyr Arg Met Ile Glu Gly Trp Arg Pro Ala					
	325		330		335	
Asp Leu Val Ser Pro	Ile Gly Asp Ile Asn Glu Gly Gln Ala Arg Glu					
	340		345		350	
Leu Ala Pro Val Leu	Lys Glu Tyr Gly Pro Glu Val Thr Val Thr Leu					
	355		360		365	
Tyr Arg Gly Val Lys	Glu Leu Arg Gly Asp Arg Arg Val Thr Ala Ala					
	370		375		380	
Asp Leu Ser Glu Ala	Arg Ala Ala Leu Pro Pro Pro Lys His Leu Ala					
	385		390		395	
Arg Pro Asp Gln Val	Arg Asp Val Leu Thr Val Ala Ala Ala Glu Gly					
	405		410		415	
Arg Ala Pro Arg Leu	Ala Pro Ala Glu Pro Lys Val Pro Ala Gln Ala					
	420		425		430	
Ala Asp Glu His Gln	Ala Glu Gln Val Asp Glu Gly Gly Val Ser Gln					
	435		440		445	
Asp Gln Val Asp Glu	Gly Ala Glu Ala Ile Ala Thr Leu Glu Ala Ala					
	450		455		460	
Val Ala Gln Gln Arg	Gln Ile Tyr Asp Arg Val Gly Gly Gly Thr Leu					
	465		470		475	
Ala Ala Ala Leu Leu	Tyr Asp Pro Gly Arg Gly Asp His Leu Arg Arg					
	485		490		495	
Glu Leu Arg Gln Tyr	Ala Gln Arg Thr Ala Tyr Arg Ala Arg Asp Thr					
	500		505		510	
Ser Gly Glu Gln Val	Ala Asp Asp Ala					
	515		520			

<210> 63  
 <211> 528  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(528)

<400> 63	
atg gga gag gcg cga gtg ccg acg agg aag cgc ggg ccg aac atg gcc	48
Met Gly Glu Ala Arg Val Pro Thr Arg Lys Arg Gly Pro Asn Met Ala	
1 5 10 15	
ctg gtc aac atg gac acc gga gag gcg gtg tcc gcc agg ccg cgg act	96
Leu Val Asn Met Asp Thr Gly Glu Ala Val Ser Ala Arg Pro Arg Thr	
20 25 30	
ccg cac cag ttc gac ggg aag ggg tac acc ttg cag gcc gta ggc agc	144
Pro His Gln Phe Asp Gly Lys Gly Tyr Thr Leu Gln Ala Val Gly Ser	
35 40 45	
gac gtc ccc ctg tac tcc ctc ggg ctg gcc gca gcg gag tgg gcg acg	192
Asp Val Pro Leu Tyr Ser Leu Gly Leu Ala Ala Ala Glu Trp Ala Thr	
50 55 60	
ctc gaa tgg ctc cgc gaa cac gga ggc gcg gcc gga tac gtc ccg gtc	240
Leu Glu Trp Leu Arg Glu His Gly Gly Ala Ala Gly Tyr Val Pro Val	
65 70 75 80	

acg ccc gag gag ctg ggc gag gac gtc ggc gcc agc aag gac acc tgc	288
Thr Pro Glu Glu Leu Gly Glu Asp Val Gly Ala Ser Lys Asp Thr Cys	
85 90 95	
cgg aag gcc ctt aac cgg ctg gtc aag ctc ggg ctt gtg gtc aag ccg	336
Arg Lys Ala Leu Asn Arg Leu Val Lys Leu Gly Leu Val Val Lys Pro	
100 105 110	
ggc ccg cga tcc ggc tct tac cag ctg aac ccc ctc cga tac tgg gag	384
Gly Pro Arg Ser Gly Ser Tyr Gln Leu Asn Pro Leu Arg Tyr Trp Glu	
115 120 125	
gga gcc ggg agc acg cag gtc aac gcc tgc cgc cgc atg gcg ccg ccg	432
Gly Ala Gly Ser Thr Gln Val Asn Ala Cys Arg Arg Met Ala Pro Pro	
130 135 140	
cgt gtg gcc ccg gac gac aag gcc atg acc agg tcc gcc agc aag ccc	480
Arg Val Ala Pro Asp Asp Lys Ala Met Thr Arg Ser Ala Ser Lys Pro	
145 150 155 160	
aag acc atc ccg gct acc cgc cgc cgc gcc gca gga gag acg cga tga	528
Lys Thr Ile Pro Ala Thr Arg Arg Arg Ala Ala Gly Glu Thr Arg *	
165 170 175	

<210> 64  
 <211> 175  
 <212> PRT  
 <213> Bacteria

<400> 64

Met Gly Glu Ala Arg Val Pro Thr Arg Lys Arg Gly Pro Asn Met Ala	
1 5 10 15	
Leu Val Asn Met Asp Thr Gly Glu Ala Val Ser Ala Arg Pro Arg Thr	
20 25 30	
Pro His Gln Phe Asp Gly Lys Gly Tyr Thr Leu Gln Ala Val Gly Ser	
35 40 45	
Asp Val Pro Leu Tyr Ser Leu Gly Leu Ala Ala Ala Glu Trp Ala Thr	
50 55 60	
Leu Glu Trp Leu Arg Glu His Gly Gly Ala Ala Gly Tyr Val Pro Val	
65 70 75 80	
Thr Pro Glu Glu Leu Gly Glu Asp Val Gly Ala Ser Lys Asp Thr Cys	
85 90 95	
Arg Lys Ala Leu Asn Arg Leu Val Lys Leu Gly Leu Val Val Lys Pro	
100 105 110	
Gly Pro Arg Ser Gly Ser Tyr Gln Leu Asn Pro Leu Arg Tyr Trp Glu	
115 120 125	
Gly Ala Gly Ser Thr Gln Val Asn Ala Cys Arg Arg Met Ala Pro Pro	
130 135 140	
Arg Val Ala Pro Asp Asp Lys Ala Met Thr Arg Ser Ala Ser Lys Pro	
145 150 155 160	
Lys Thr Ile Pro Ala Thr Arg Arg Arg Ala Ala Gly Glu Thr Arg	
165 170 175	

<210> 65

<211> 420  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(420)

<400> 65  
 atg acg acc atg ccc gta gaa ggc ttc aac ccg gag cgc gac ctg acc 48  
 Met Thr Thr Met Pro Val Glu Gly Phe Asn Pro Glu Arg Asp Leu Thr  
 1 5 10 15

gcc ccg tcg ctg tac tcg ctg aac ctg tcc gcc gct cag cac tgc acg 96  
 Ala Pro Ser Leu Tyr Ser Leu Asn Leu Ser Ala Ala Gln His Cys Thr  
 20 25 30

ctc gcg tgg gtg gag gac cac ggc ggc ctg ttt gac gtc atc ccc gta 144  
 Leu Ala Trp Val Glu Asp His Gly Gly Leu Phe Asp Val Ile Pro Val  
 35 40 45

ccg gtc gaa acc gtc gcc gag gac tgc ggc aac tcc gtc tcc acg gtg 192  
 Pro Val Glu Thr Val Ala Glu Asp Cys Gly Asn Ser Val Ser Thr Val  
 50 55 60

cac gag gct ctc gcc cgc ctg gag gcc ctg aac ctc ctc gtg cgg acc 240  
 His Glu Ala Leu Ala Arg Leu Glu Ala Leu Asn Leu Leu Val Arg Thr  
 65 70 75 80

tcc gcc ggc ctc tac cgg atc aac gcc cgg tac tac ttc acg ctg cac 288  
 Ser Ala Gly Leu Tyr Arg Ile Asn Ala Arg Tyr Tyr Phe Thr Leu His  
 85 90 95

ccc gag ctg cgc gag atg atc acc gcc gcc ctc acg gac ccc ccg gtc 336  
 Pro Glu Leu Arg Glu Met Ile Thr Ala Ala Leu Thr Asp Pro Pro Val  
 100 105 110

acc ccg gac gac cgt gcc cgc gcg ccc cgc aag gtc agc aac acc gac 384  
 Thr Pro Asp Asp Arg Ala Arg Ala Pro Arg Lys Val Ser Asn Thr Asp  
 115 120 125

gct cgc cgc cgc cgg acg atc cgc ccc gtc tct tga 420  
 Ala Arg Arg Arg Arg Thr Ile Arg Pro Val Ser \*  
 130 135

<210> 66  
 <211> 139  
 <212> PRT  
 <213> Bacteria

<400> 66  
 Met Thr Thr Met Pro Val Glu Gly Phe Asn Pro Glu Arg Asp Leu Thr  
 1 5 10 15  
 Ala Pro Ser Leu Tyr Ser Leu Asn Leu Ser Ala Ala Gln His Cys Thr  
 20 25 30  
 Leu Ala Trp Val Glu Asp His Gly Gly Leu Phe Asp Val Ile Pro Val  
 35 40 45

Pro	Val	Glu	Thr	Val	Ala	Glu	Asp	Cys	Gly	Asn	Ser	Val	Ser	Thr	Val
50						55				60					
His	Glu	Ala	Leu	Ala	Arg	Leu	Glu	Ala	Leu	Asn	Leu	Leu	Val	Arg	Thr
65					70					75					80
Ser	Ala	Gly	Leu	Tyr	Arg	Ile	Asn	Ala	Arg	Tyr	Tyr	Phe	Thr	Leu	His
			85						90					95	
Pro	Glu	Leu	Arg	Glu	Met	Ile	Thr	Ala	Ala	Leu	Thr	Asp	Pro	Pro	Val
			100					105					110		
Thr	Pro	Asp	Asp	Arg	Ala	Arg	Ala	Pro	Arg	Lys	Val	Ser	Asn	Thr	Asp
		115					120					125			
Ala	Arg	Arg	Arg	Arg	Thr	Ile	Arg	Pro	Val	Ser					
130							135								

<210> 67  
 <211> 564  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(564)

<400> 67																
gtg	cca	gac	ggt	cag	ttg	ccg	ccc	tgt	acg	gga	gga	agc	tcg	aag	cct	48
Val	Pro	Asp	Gly	Gln	Leu	Pro	Pro	Cys	Thr	Gly	Gly	Ser	Ser	Lys	Pro	
1				5					10					15		
tca ggc tgc tcg tgt cca tcg cca acg agc gtc tgc gtc acg gcc agg															96	
Ser	Gly	Cys	Ser	Cys	Pro	Ser	Pro	Thr	Ser	Val	Cys	Val	Thr	Ala	Arg	
			20					25					30			
acg tcg ccc ttc gcg tcg tac tgg acg gtc cgg tac agc atc aca ggc															144	
Thr	Ser	Pro	Phe	Ala	Ser	Tyr	Trp	Thr	Val	Arg	Tyr	Ser	Ile	Thr	Gly	
			35				40					45				
ttg ctc gcg gag ggc gga agg ccg aag tct tcg cac tcg aac cag gcg															192	
Leu	Leu	Ala	Glu	Gly	Gly	Arg	Pro	Lys	Ser	Ser	His	Ser	Asn	Gln	Ala	
		50				55					60					
agc atc cga gcg gtc agg gtg cgc tcc agc cgg acg cac ccc gga atc															240	
Ser	Ile	Arg	Ala	Val	Arg	Val	Arg	Ser	Ser	Arg	Thr	His	Pro	Gly	Ile	
	65				70				75					80		
gtg ggg gcc aca ggc gtt aga gcc agg tcc ggc gag acg cgc ggc ggc															288	
Val	Gly	Ala	Thr	Gly	Val	Arg	Ala	Arg	Ser	Gly	Glu	Thr	Arg	Gly	Gly	
				85					90					95		
ggg atc ggg agc cca aga cct ggc gca agc ctc cgc acc gtc tca ctc															336	
Gly	Ile	Gly	Ser	Pro	Arg	Pro	Gly	Ala	Ser	Leu	Arg	Thr	Val	Ser	Leu	
			100					105					110			
acg acg gcc acc ggg tca cca agg ctg gtc agg tcg aac cac tcg ccc															384	
Thr	Thr	Ala	Thr	Gly	Ser	Pro	Arg	Leu	Val	Arg	Ser	Asn	His	Ser	Pro	
		115					120					125				
cgc cgg ttg tgc tca cgg aac tcc tgg tgg agc gcc ccc tca agg gcg															432	
Arg	Arg	Leu	Cys	Ser	Arg	Asn	Ser	Trp	Trp	Ser	Ala	Pro	Ser	Arg	Ala	

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130              135              140
cgg ccg ccc tcg cac gtc cac agc acc gac agc gtc agc ggc aga ccg 480
Arg Pro Pro Ser His Val His Ser Thr Asp Ser Val Ser Gly Arg Pro
145              150              155              160

gtc tgc atc gtg cgg act ctc ctc tcc acg tct gtc gtg gtg ccg atc 528
Val Cys Ile Val Arg Thr Leu Leu Ser Thr Ser Val Val Val Pro Ile
165              170              175

ttc acc agg tct agg ccc tcg gct cct aag aga tag 564
Phe Thr Arg Ser Arg Pro Ser Ala Pro Lys Arg *
180              185

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<210> 68  
 <211> 187  
 <212> PRT  
 <213> Bacteria

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<400> 68
Val Pro Asp Gly Gln Leu Pro Pro Cys Thr Gly Gly Ser Ser Lys Pro
1      5      10      15
Ser Gly Cys Ser Cys Pro Ser Pro Thr Ser Val Cys Val Thr Ala Arg
20     25     30
Thr Ser Pro Phe Ala Ser Tyr Trp Thr Val Arg Tyr Ser Ile Thr Gly
35     40     45
Leu Leu Ala Glu Gly Gly Arg Pro Lys Ser Ser His Ser Asn Gln Ala
50     55     60
Ser Ile Arg Ala Val Arg Val Arg Ser Ser Arg Thr His Pro Gly Ile
65     70     75     80
Val Gly Ala Thr Gly Val Arg Ala Arg Ser Gly Glu Thr Arg Gly Gly
85     90     95
Gly Ile Gly Ser Pro Arg Pro Gly Ala Ser Leu Arg Thr Val Ser Leu
100    105    110
Thr Thr Ala Thr Gly Ser Pro Arg Leu Val Arg Ser Asn His Ser Pro
115    120    125
Arg Arg Leu Cys Ser Arg Asn Ser Trp Trp Ser Ala Pro Ser Arg Ala
130    135    140
Arg Pro Pro Ser His Val His Ser Thr Asp Ser Val Ser Gly Arg Pro
145    150    155    160
Val Cys Ile Val Arg Thr Leu Leu Ser Thr Ser Val Val Val Pro Ile
165    170    175
Phe Thr Arg Ser Arg Pro Ser Ala Pro Lys Arg
180    185

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<210> 69  
 <211> 798  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1) ... (798)

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<400> 69
atg gcg act agg cgg aag ggc cgc cct ggc ggc tat gag gaa atc gcc 48

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Met	Ala	Thr	Arg	Arg	Lys	Gly	Arg	Pro	Gly	Gly	Tyr	Glu	Glu	Ile	Ala		
1				5					10					15			
gcg	cac	ttt	cgg	cgg	ctc	atg	gac	tcg	ggc	gag	ttg	tcc	cct	ggc	gac	96	
Ala	His	Phe	Arg	Arg	Leu	Met	Asp	Ser	Gly	Glu	Leu	Ser	Pro	Gly	Asp		
			20					25					30				
ccg	ctg	ccc	tcc	atg	cgc	gac	gtg	tgc	gac	cag	ttc	ggt	tgc	gcg	atc	144	
Pro	Leu	Pro	Ser	Met	Arg	Asp	Val	Cys	Asp	Gln	Phe	Gly	Ser	Ala	Ile		
			35				40					45					
acg	acg	gtg	aac	cgg	gcg	ttc	cgg	ctc	ctc	cag	gag	gag	ggc	cgg	acg	192	
Thr	Thr	Val	Asn	Arg	Ala	Phe	Arg	Leu	Leu	Gln	Glu	Glu	Gly	Arg	Thr		
		50				55				60							
gtc	tcc	aag	ccg	ggc	gtg	ggc	acg	atc	gtc	cgg	gac	atg	tcc	cgg	gtt	240	
Val	Ser	Lys	Pro	Gly	Val	Gly	Thr	Ile	Val	Arg	Asp	Met	Ser	Arg	Val		
65					70				75					80			
cgg	gtg	ccg	ttc	agt	acg	tac	ggc	gac	gtc	ctg	gcg	ccg	ggc	ggc	gat	288	
Arg	Val	Pro	Phe	Ser	Thr	Tyr	Gly	Asp	Val	Leu	Ala	Pro	Gly	Gly	Asp		
				85				90					95				
aag	ggc	ccg	tgg	gag	cgt	gcg	acg	gcc	gcg	cag	ggc	ctt	gac	ggc	cgg	336	
Lys	Gly	Pro	Trp	Glu	Arg	Ala	Thr	Ala	Ala	Gln	Gly	Leu	Asp	Gly	Arg		
			100					105					110				
atg	ctc	gtg	gag	gcg	ccc	gag	gag	gtc	ggg	gcc	ccg	gcg	gac	gtc	gcc	384	
Met	Leu	Val	Glu	Ala	Pro	Glu	Glu	Val	Gly	Ala	Pro	Ala	Asp	Val	Ala		
			115				120					125					
gcg	cgc	ctc	ggc	atc	gag	ccg	ggc	gcc	ctg	gtc	gtc	cac	cgg	cgg	cgc	432	
Ala	Arg	Leu	Gly	Ile	Glu	Pro	Gly	Ala	Leu	Val	Val	His	Arg	Arg	Arg		
		130				135					140						
cgc	gcc	acg	atc	ggc	gag	gac	gtc	gtc	cag	ctc	caa	gac	gcc	tgg	tac	480	
Arg	Ala	Thr	Ile	Gly	Glu	Asp	Val	Val	Gln	Leu	Gln	Asp	Ala	Trp	Tyr		
145					150				155					160			
ccg	ctg	gag	atc	gcc	cgg	gcc	gcc	ggc	ctg	gac	cgg	ccg	ggg	aag	gtc	528	
Pro	Leu	Glu	Ile	Ala	Arg	Ala	Ala	Gly	Leu	Asp	Arg	Pro	Gly	Lys	Val		
				165				170						175			
gtg	ggt	ggt	gtc	ctc	ggt	gcc	atg	acg	ggc	gcc	ggc	ctt	tgc	ccg	acg	576	
Val	Gly	Gly	Val	Leu	Gly	Ala	Met	Thr	Gly	Ala	Gly	Leu	Ser	Pro	Thr		
			180					185					190				
tcc	acc	gac	cac	gac	gtc	gag	gtg	tgg	gtg	ccg	tcc	gcg	cag	caa	gcc	624	
Ser	Thr	Asp	His	Asp	Val	Glu	Val	Trp	Val	Pro	Ser	Ala	Gln	Gln	Ala		
			195				200					205					
gcg	gaa	ctc	tcc	ctc	ggc	tcc	cgc	gtg	tgc	gtc	ctg	gtc	gtc	gag	cgc	672	
Ala	Glu	Leu	Ser	Leu	Gly	Ser	Arg	Val	Ser	Val	Leu	Val	Val	Glu	Arg		
		210				215					220						
gtc	acc	tac	gac	gcg	acg	gtc	cgt	gtc	ctg	gaa	ctg	acc	cgt	cac	acg	720	
Val	Thr	Tyr	Asp	Ala	Thr	Val	Arg	Val	Leu	Glu	Leu	Thr	Arg	His	Thr		
225					230				235						240		



ggc gcg gct gac agg ctg acg ctg acc tac aag ggc ctg cca ctc cgg 768  
 Gly Ala Ala Asp Arg Leu Thr Leu Thr Tyr Lys Gly Leu Pro Leu Arg  
                   245                                  250                                  255

gcg acc gga gcc gag ggg agc acg tca tga 798  
 Ala Thr Gly Ala Glu Gly Ser Thr Ser \*  
                   260                                  265

<210> 70  
 <211> 265  
 <212> PRT  
 <213> Bacteria

<400> 70  
 Met Ala Thr Arg Arg Lys Gly Arg Pro Gly Gly Tyr Glu Glu Ile Ala  
   1                  5                  10                  15  
 Ala His Phe Arg Arg Leu Met Asp Ser Gly Glu Leu Ser Pro Gly Asp  
                   20                  25                  30  
 Pro Leu Pro Ser Met Arg Asp Val Cys Asp Gln Phe Gly Ser Ala Ile  
                   35                  40                  45  
 Thr Thr Val Asn Arg Ala Phe Arg Leu Leu Gln Glu Glu Gly Arg Thr  
                   50                  55                  60  
 Val Ser Lys Pro Gly Val Gly Thr Ile Val Arg Asp Met Ser Arg Val  
   65                  70                  75                  80  
 Arg Val Pro Phe Ser Thr Tyr Gly Asp Val Leu Ala Pro Gly Gly Asp  
                   85                  90                  95  
 Lys Gly Pro Trp Glu Arg Ala Thr Ala Ala Gln Gly Leu Asp Gly Arg  
                   100                  105                  110  
 Met Leu Val Glu Ala Pro Glu Glu Val Gly Ala Pro Ala Asp Val Ala  
                   115                  120                  125  
 Ala Arg Leu Gly Ile Glu Pro Gly Ala Leu Val Val His Arg Arg Arg  
                   130                  135                  140  
 Arg Ala Thr Ile Gly Glu Asp Val Val Gln Leu Gln Asp Ala Trp Tyr  
   145                  150                  155                  160  
 Pro Leu Glu Ile Ala Arg Ala Ala Gly Leu Asp Arg Pro Gly Lys Val  
                   165                  170                  175  
 Val Gly Gly Val Leu Gly Ala Met Thr Gly Ala Gly Leu Ser Pro Thr  
                   180                  185                  190  
 Ser Thr Asp His Asp Val Glu Val Trp Val Pro Ser Ala Gln Gln Ala  
                   195                  200                  205  
 Ala Glu Leu Ser Leu Gly Ser Arg Val Ser Val Leu Val Val Glu Arg  
                   210                  215                  220  
 Val Thr Tyr Asp Ala Thr Val Arg Val Leu Glu Leu Thr Arg His Thr  
   225                  230                  235                  240  
 Gly Ala Ala Asp Arg Leu Thr Leu Thr Tyr Lys Gly Leu Pro Leu Arg  
                   245                  250                  255  
 Ala Thr Gly Ala Glu Gly Ser Thr Ser  
                   260                                  265

<210> 71  
 <211> 378  
 <212> DNA  
 <213> Bacteria

<220>

<221> CDS

<222> (1)...(378)

<400> 71

atg tcc acg acc acc aac gcg gtc acc tgg ttc gag gtc ggc acc gac	48
Met Ser Thr Thr Thr Asn Ala Val Thr Trp Phe Glu Val Gly Thr Asp	
1 5 10 15	
cgg ccg gag gag acc ggg cgc ttc tac gcc gac ctg ttc ggt tgg gcg	96
Arg Pro Glu Glu Thr Gly Arg Phe Tyr Ala Asp Leu Phe Gly Trp Ala	
20 25 30	
ttc ggc gag cag ggg acg ccg gag gcg tcg tac cgg gtg acg gag ccg	144
Phe Gly Glu Gln Gly Thr Pro Glu Ala Ser Tyr Arg Val Thr Glu Pro	
35 40 45	
ggg ccg gag ggc tcg atc cag ggc gcg atc cgg ggc acc ggc ggg gcg	192
Gly Pro Glu Gly Ser Ile Gln Gly Ala Ile Arg Gly Thr Gly Gly Ala	
50 55 60	
agc ccg aac tac gcc atc ttc tac gtg cag gtg gcc gac gtg gcg gac	240
Ser Pro Asn Tyr Ala Ile Phe Tyr Val Gln Val Ala Asp Val Ala Asp	
65 70 75 80	
gcc tgc ccg cgc gcg gag gcg gcc ggt ggc aag gtg ctg gtg ccg gcg	288
Ala Cys Arg Arg Ala Glu Ala Ala Gly Gly Lys Val Leu Val Pro Ala	
85 90 95	
aag tcc acc gac aac ggg ctc acc ttc gcc cac ctg ctc gac ccg gtc	336
Lys Ser Thr Asp Asn Gly Leu Thr Phe Ala His Leu Leu Asp Pro Val	
100 105 110	
ggc aac cac ttc ggc gtc ttc gcc ccg ccg ccg gcc gcc tga	378
Gly Asn His Phe Gly Val Phe Ala Pro Pro Pro Ala Ala *	
115 120 125	

<210> 72

<211> 125

<212> PRT

<213> Bacteria

<400> 72

Met Ser Thr Thr Thr Asn Ala Val Thr Trp Phe Glu Val Gly Thr Asp	
1 5 10 15	
Arg Pro Glu Glu Thr Gly Arg Phe Tyr Ala Asp Leu Phe Gly Trp Ala	
20 25 30	
Phe Gly Glu Gln Gly Thr Pro Glu Ala Ser Tyr Arg Val Thr Glu Pro	
35 40 45	
Gly Pro Glu Gly Ser Ile Gln Gly Ala Ile Arg Gly Thr Gly Gly Ala	
50 55 60	
Ser Pro Asn Tyr Ala Ile Phe Tyr Val Gln Val Ala Asp Val Ala Asp	
65 70 75 80	
Ala Cys Arg Arg Ala Glu Ala Ala Gly Gly Lys Val Leu Val Pro Ala	
85 90 95	
Lys Ser Thr Asp Asn Gly Leu Thr Phe Ala His Leu Leu Asp Pro Val	
100 105 110	

Gly Asn His Phe Gly Val Phe Ala Pro Pro Pro Ala Ala  
 115 120 125

<210> 73  
 <211> 741  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(741)

<400> 73  
 gtg cgg cga cgg cct gaa tcg tgg ggc cgg aag ccg gag ccg ccg tcc 48  
 Val Arg Arg Arg Pro Glu Ser Trp Gly Arg Lys Pro Glu Pro Pro Ser  
 1 5 10 15

gcc ccg gcg agg ttg ccg ggg cgg acg gcg tac ggt cac ttg ccg gcc 96  
 Ala Pro Ala Arg Leu Pro Gly Arg Thr Ala Tyr Gly His Leu Pro Ala  
 20 25 30

gag cct ccg cga ccg ccc ggg ccg gcc agg acg ccg gcc tcg gcg gcc 144  
 Glu Pro Pro Arg Pro Pro Gly Pro Ala Arg Thr Pro Ala Ser Ala Ala  
 35 40 45

gcg gtg atc gcg tcc gcc tgc tcc tgg gtg agc ttg ccg tcc tcg acc 192  
 Ala Val Ile Ala Ser Ala Cys Ser Trp Val Ser Leu Pro Ser Ser Thr  
 50 55 60

gcc tgc gcc agg cgc tcc ttc agc gcg gcc tgc cgg tcg gcg gag tca 240  
 Ala Cys Ala Arg Arg Ser Phe Ser Ala Ala Cys Arg Ser Ala Glu Ser  
 65 70 75 80

ccc cgc tcg ggc cgg tcg gcc ggc ttc tgc gcc tcg cgc acc ttc tcc 288  
 Pro Arg Ser Gly Arg Ser Ala Gly Phe Cys Ala Ser Arg Thr Phe Ser  
 85 90 95

agc gcg gcc gtc acc ttg tcg gtg tcg acg ccc agc tcc ttg gcc agg 336  
 Ser Ala Ala Val Thr Leu Ser Val Ser Thr Pro Ser Ser Leu Ala Arg  
 100 105 110

gcc tcg gcg aac tcc gcc tgc cgc tcg gcc cgc tgc tgc tgc cgc tcg 384  
 Ala Ser Ala Asn Ser Ala Cys Arg Ser Ala Arg Cys Cys Cys Arg Ser  
 115 120 125

tca ctg ctg ctg ccg ctc tcg ctc gcg ctg gcg ctc ggc gtc gcg gtg 432  
 Ser Leu Leu Leu Pro Leu Ser Leu Ala Leu Ala Leu Gly Val Ala Val  
 130 135 140

ccg ccg tcc gcg gcg aac gcg acc gtc ggc gcc gcg atc ccc acg ccg 480  
 Pro Pro Ser Ala Ala Asn Ala Thr Val Gly Ala Ala Ile Pro Thr Pro  
 145 150 155 160

aga acc ccg gcc gcg gcc agg ccg gcc agc agg tgc ttc ttc ttc atg 528  
 Arg Thr Pro Ala Ala Ala Arg Pro Ala Ser Arg Cys Phe Phe Phe Met  
 165 170 175



<210> 75  
 <211> 891  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(891)

<400> 75  
 gtg atc ctc gtg gcg ttg gcg aag atc cgg gaa gtc ccg ctc acc ggg 48  
 Val Ile Leu Val Ala Leu Ala Lys Ile Arg Glu Val Pro Leu Thr Gly  
 1 5 10 15

gcg gac gcc ggc ccg tac ggc gtc acc gtc ggc ccc gac ggc gcg ctc 96  
 Ala Asp Ala Gly Pro Tyr Gly Val Thr Val Gly Pro Asp Gly Ala Leu  
 20 25 30

tgg ctg acg ctg gtc cac gcc ggc gcg gtc gcc cgg gtg ggc gcg gac 144  
 Trp Leu Thr Leu Val His Ala Gly Ala Val Ala Arg Val Gly Ala Asp  
 35 40 45

ggc gac ctg cgc acc tgg cag gtg gcg gcc gac agc cgg ccg ctg atc 192  
 Gly Asp Leu Arg Thr Trp Gln Val Ala Ala Asp Ser Arg Pro Leu Ile  
 50 55 60

gtc acg ccg ggc ccc gac ggc gcc ctc tgg ttc acc cgc tcc ggc gac 240  
 Val Thr Pro Gly Pro Asp Gly Ala Leu Trp Phe Thr Arg Ser Gly Asp  
 65 70 75 80

gac cgg atc ggc cgg atc acc acc gac ggg gag cag agc gcc gtc gcg 288  
 Asp Arg Ile Gly Arg Ile Thr Thr Asp Gly Glu Gln Ser Ala Val Ala  
 85 90 95

ctc ccg ccc ggg agc ggc ccc tgc ggc atc gcc gcc ggt ccc gac ggc 336  
 Leu Pro Pro Gly Ser Gly Pro Cys Gly Ile Ala Ala Gly Pro Asp Gly  
 100 105 110

gcc ctc tgg tac gcg gcg atg acc gcc gac gcg gtc ggc cgc gtc acc 384  
 Ala Leu Trp Tyr Ala Ala Met Thr Ala Asp Ala Val Gly Arg Val Thr  
 115 120 125

acc gac ggg aag gtg acg cag ttt ccg ctg ccg gtg agc ggc ggc ttc 432  
 Thr Asp Gly Lys Val Thr Gln Phe Pro Leu Pro Val Ser Gly Gly Phe  
 130 135 140

gcc tcg atg gtc gcc gcc ggc ccg gac gag gcc gtc tgg ttc acg ctc 480  
 Ala Ser Met Val Ala Ala Gly Pro Asp Glu Ala Val Trp Phe Thr Leu  
 145 150 155 160

aac cag gcg aac gcg gtc ggc cgg atc ggc acg gac ggc gcg gtg gcg 528  
 Asn Gln Ala Asn Ala Val Gly Arg Ile Gly Thr Asp Gly Ala Val Ala  
 165 170 175

ctg cac cca ctg ccg acc gag ggc gcc gcc ccg gtg ggc atc acg gcc 576



<212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(1086)

<400> 77

gtg acc gcg gcg ggc ccc gag cgc ctc cac cgg cgc ggc ggc ggc ctc	48
Val Thr Ala Ala Gly Pro Glu Arg Leu His Arg Arg Gly Gly Gly Leu	
1 5 10 15	
ccc cgg ccg acc gga gca ggc gtc cca cgc tcg gcg gag tgg gcc gac	96
Pro Arg Pro Thr Gly Ala Gly Val Pro Arg Ser Ala Glu Trp Ala Asp	
20 25 30	
cgg tac gtg ggc ggc gcc ccg ccg cga cta ggc tct gcc gct gtg tcc	144
Arg Tyr Val Gly Gly Ala Pro Pro Arg Leu Gly Ser Ala Ala Val Ser	
35 40 45	
gac cat gcc agc acg act ccc gcc acc gcc gta cga ccg ccg gtg ctg	192
Asp His Ala Ser Thr Thr Pro Ala Thr Ala Val Arg Pro Pro Val Leu	
50 55 60	
tgc ccc ggc gac acg gtg atg ctg gtg tcg ccg tcg ggg ccg acc cgg	240
Cys Pro Gly Asp Thr Val Met Leu Val Ser Pro Ser Gly Pro Thr Arg	
65 70 75 80	
ccc gag cgg gtg gcc cgg ggc atc gag ctg ctc acc ggc tgg ggg ctg	288
Pro Glu Arg Val Ala Arg Gly Ile Glu Leu Leu Thr Gly Trp Gly Leu	
85 90 95	
cgg ccg gtg ctg gcg ccg aac gcg tac gcc cgg cag ggt tac ctg gcc	336
Arg Pro Val Leu Ala Pro Asn Ala Tyr Ala Arg Gln Gly Tyr Leu Ala	
100 105 110	
ggc gcg gac gag ctg cgc gcc gcc gac ctg aac gcg gcg ttc gcc gac	384
Gly Ala Asp Glu Leu Arg Ala Ala Asp Leu Asn Ala Ala Phe Ala Asp	
115 120 125	
ccc gag gtg cgc ggg gtg atc tgc acg cgc gcc ggg tac gcc gcg cag	432
Pro Glu Val Arg Gly Val Ile Cys Thr Arg Gly Gly Tyr Gly Ala Gln	
130 135 140	
cgg atc gtc gac gcg atc gac atg gcc gcc gta cgc cgg gac ccg aag	480
Arg Ile Val Asp Ala Ile Asp Met Ala Ala Val Arg Arg Asp Pro Lys	
145 150 155 160	
gtg gtc gcc ggg ttc tcc gac atc acc gcg ctg cag ctc gcg ctg tgg	528
Val Val Ala Gly Phe Ser Asp Ile Thr Ala Leu Gln Leu Ala Leu Trp	
165 170 175	
cgg ggc gcc cgg ctg gcc ggc gtg cac gcc ccc ggg gcg gcg tgg ctg	576
Arg Gly Ala Arg Leu Ala Gly Val His Gly Pro Gly Ala Ala Trp Leu	
180 185 190	
gac gag cgc act ccg ctg cgg tcg gcc gag tcg ctg cac gcc gcc ctg	624
Asp Glu Arg Thr Pro Leu Arg Ser Ala Glu Ser Leu His Ala Ala Leu	

195	200	205	
atg acc acc gaa ccg gtg acg gtg acc gcc gtc gcc gag gag gag acg			672
Met Thr Thr Glu Pro Val Thr Val Thr Ala Val Ala Glu Glu Glu Thr			
210	215	220	
ttc ccg gtg ccg gtg ccc ggg ccg gcc acc ggc ccg ctg ctg ggc ggc			720
Phe Pro Val Arg Val Pro Gly Arg Ala Thr Gly Pro Leu Leu Gly Gly			
225	230	235	240
aac ctc tgc ctg gtc gtg gcg tcg ctg ggc acc ccg gac atg ccg gac			768
Asn Leu Cys Leu Val Val Ala Ser Leu Gly Thr Pro Asp Met Pro Asp			
245	250	255	
ctg acc ggc gcg atc ctg ttg atc gag gac gtg cag gag ccg ccg tac			816
Leu Thr Gly Ala Ile Leu Leu Ile Glu Asp Val Gln Glu Pro Pro Tyr			
260	265	270	
aag gtg gac ccg atg ctc acc cag ttg cgc ccg gcc ggc gcg ctg gac			864
Lys Val Asp Arg Met Leu Thr Gln Leu Arg Arg Ala Gly Ala Leu Asp			
275	280	285	
ggg ctg gcc ggg gtg gcg gtc ggc cag ttc acc ggc tgc gcc gac ggc			912
Gly Leu Ala Gly Val Ala Val Gly Gln Phe Thr Gly Cys Ala Asp Gly			
290	295	300	
tgg tcg acc agc gtc gcc gac gtg ctc tcc gag cgc ctc ggc gac ctc			960
Trp Ser Thr Ser Val Ala Asp Val Leu Ser Glu Arg Leu Gly Asp Leu			
305	310	315	320
ggc gtc ccg gtc ctc ggc ggc ctg ccc gtc ggc cac ggc gtc ggc cag			1008
Gly Val Pro Val Leu Gly Gly Leu Pro Val Gly His Gly Val Gly Gln			
325	330	335	
ctc acc gtc ccg gtc ggc acc gac gcg acc ctc gac acg acg acg gcc			1056
Leu Thr Val Pro Val Gly Thr Asp Ala Thr Leu Asp Thr Thr Thr Ala			
340	345	350	
acc ctc acg gtc acc ccc gcc gtc cgc tga			1086
Thr Leu Thr Val Thr Pro Ala Val Arg *			
355	360		

<210> 78  
 <211> 361  
 <212> PRT  
 <213> Bacteria

<400> 78  
 Val Thr Ala Ala Gly Pro Glu Arg Leu His Arg Arg Gly Gly Gly Leu  
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 20 25 30  
 Arg Tyr Val Gly Gly Ala Pro Pro Arg Leu Gly Ser Ala Ala Val Ser  
 35 40 45  
 Asp His Ala Ser Thr Thr Pro Ala Thr Ala Val Arg Pro Pro Val Leu  
 50 55 60  
 Cys Pro Gly Asp Thr Val Met Leu Val Ser Pro Ser Gly Pro Thr Arg



65					70					75					80
Pro	Glu	Arg	Val	Ala	Arg	Gly	Ile	Glu	Leu	Leu	Thr	Gly	Trp	Gly	Leu
				85					90					95	
Arg	Pro	Val	Leu	Ala	Pro	Asn	Ala	Tyr	Ala	Arg	Gln	Gly	Tyr	Leu	Ala
			100					105					110		
Gly	Ala	Asp	Glu	Leu	Arg	Ala	Ala	Asp	Leu	Asn	Ala	Ala	Phe	Ala	Asp
		115					120					125			
Pro	Glu	Val	Arg	Gly	Val	Ile	Cys	Thr	Arg	Gly	Gly	Tyr	Gly	Ala	Gln
	130					135					140				
Arg	Ile	Val	Asp	Ala	Ile	Asp	Met	Ala	Ala	Val	Arg	Arg	Asp	Pro	Lys
145					150					155					160
Val	Val	Ala	Gly	Phe	Ser	Asp	Ile	Thr	Ala	Leu	Gln	Leu	Ala	Leu	Trp
			165					170						175	
Arg	Gly	Ala	Arg	Leu	Ala	Gly	Val	His	Gly	Pro	Gly	Ala	Ala	Trp	Leu
		180						185					190		
Asp	Glu	Arg	Thr	Pro	Leu	Arg	Ser	Ala	Glu	Ser	Leu	His	Ala	Ala	Leu
	195						200					205			
Met	Thr	Thr	Glu	Pro	Val	Thr	Val	Thr	Ala	Val	Ala	Glu	Glu	Glu	Thr
	210					215					220				
Phe	Pro	Val	Arg	Val	Pro	Gly	Arg	Ala	Thr	Gly	Pro	Leu	Leu	Gly	Gly
225				230						235					240
Asn	Leu	Cys	Leu	Val	Val	Ala	Ser	Leu	Gly	Thr	Pro	Asp	Met	Pro	Asp
			245						250					255	
Leu	Thr	Gly	Ala	Ile	Leu	Leu	Ile	Glu	Asp	Val	Gln	Glu	Pro	Pro	Tyr
		260						265					270		
Lys	Val	Asp	Arg	Met	Leu	Thr	Gln	Leu	Arg	Arg	Ala	Gly	Ala	Leu	Asp
	275					280					285				
Gly	Leu	Ala	Gly	Val	Ala	Val	Gly	Gln	Phe	Thr	Gly	Cys	Ala	Asp	Gly
	290					295					300				
Trp	Ser	Thr	Ser	Val	Ala	Asp	Val	Leu	Ser	Glu	Arg	Leu	Gly	Asp	Leu
305				310						315					320
Gly	Val	Pro	Val	Leu	Gly	Gly	Leu	Pro	Val	Gly	His	Gly	Val	Gly	Gln
			325					330					335		
Leu	Thr	Val	Pro	Val	Gly	Thr	Asp	Ala	Thr	Leu	Asp	Thr	Thr	Thr	Ala
		340					345						350		
Thr	Leu	Thr	Val	Thr	Pro	Ala	Val	Arg							
	355					360									

<210> 79  
 <211> 861  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(861)

<400> 79	
gtg gga cgc ctg ctc cgg tcg gcc ggg gga ggc cgc cgc cgc gcc ggt	48
Val Gly Arg Leu Leu Arg Ser Ala Gly Gly Gly Arg Arg Arg Ala Gly	
1 5 10 15	
gga ggc gct cgg ggc ccg ccg cgg tca ccg gct agc ctc gac gtc gtg	96
Gly Gly Ala Arg Gly Pro Pro Arg Ser Pro Ala Ser Leu Asp Val Val	
20 25 30	
gct acc gcg ttg gtg atc gag aac gac ccg acc gac gac gtc cgc cgg	144

**Table 1.** Mean values of the variables measured during the study

gac gac gac acg tcc cgc cgc agc ctg ccg ctg ctc ggg cag tga 861  
 Asp Asp Asp Thr Ser Arg Arg Ser Leu Pro Leu Leu Gly Gln \*  
 275 280 285

<210> 80  
 <211> 286  
 <212> PRT  
 <213> Bacteria

<400> 80  
 Val Gly Arg Leu Leu Arg Ser Ala Gly Gly Gly Arg Arg Arg Ala Gly  
 1 5 10 15  
 Gly Gly Ala Arg Gly Pro Pro Arg Ser Pro Ala Ser Leu Asp Val Val  
 20 25 30  
 Ala Thr Ala Leu Val Ile Glu Asn Asp Pro Thr Asp Asp Val Arg Arg  
 35 40 45  
 Leu Gly Glu Trp Leu Thr Glu Ala Gly Leu Asp Leu Trp Val Val Arg  
 50 55 60  
 Ala His Ala Gly Asp Gln Leu Pro Ala Asp Leu Glu Gly Tyr Ser Ala  
 65 70 75 80  
 Leu Val Val Leu Gly Gly Glu Gln Gln Ala Tyr Pro Leu Pro Asp Gly  
 85 90 95  
 Ser Pro Gly Ala Pro Trp Phe Pro Ala Val Glu Gly Leu Leu Arg Lys  
 100 105 110  
 Ala Val Arg Asp Arg Val Pro Thr Leu Gly Ile Cys Leu Gly Ala Gln  
 115 120 125  
 Leu Leu Ala Thr Ala His Ala Gly Glu Val Glu Arg Ser Ala Ser Gly  
 130 135 140  
 Pro Glu Val Gly Pro Gly Val Val Gly Lys Arg Asp Ala Ala Asp Ala  
 145 150 155 160  
 Asp Pro Leu Phe Arg Tyr Val Pro Leu Ile Pro Asp Val Leu Gln Trp  
 165 170 175  
 His Ala Asp Glu Ile Thr Glu Leu Pro Arg Gly Ala Thr Leu Leu Ala  
 180 185 190  
 Ala Ser Thr Arg Tyr Pro His Gln Ala Phe Arg Leu Gly Asp Arg Ala  
 195 200 205  
 Trp Gly Leu Gln Phe His Ile Glu Cys Asp Thr Ala Met Ile Ala Asp  
 210 215 220  
 Trp Ala Thr Asp Ser Thr Leu Leu Ala Glu Leu Gly Tyr Asp Pro Asp  
 225 230 235 240  
 Leu Val Val Ala Ala Cys His Ala Val Met Val Asp Val Glu Glu Val  
 245 250 255  
 Trp Gln Pro Phe Ala Ala Arg Phe Ala Ala Leu Ala Leu Gly Glu Leu  
 260 265 270  
 Asp Asp Asp Thr Ser Arg Arg Ser Leu Pro Leu Leu Gly Gln  
 275 280 285

<210> 81  
 <211> 3033  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS

<222> (1)...(3033)

<400> 81

gtg	atg	agc	cgg	ccg	acc	agc	gcc	gcc	gga	cgg	ctc	gcc	cgc	tac	ggc	48
Val	Met	Ser	Arg	Pro	Thr	Ser	Ala	Ala	Gly	Arg	Leu	Ala	Arg	Tyr	Gly	
1				5					10					15		
ttc	ggc	atc	gtc	ggc	ggc	gac	ggc	gcc	acc	cgc	gcc	gcc	gac	ctg	ctc	96
Phe	Gly	Ile	Val	Gly	Gly	Asp	Gly	Ala	Thr	Arg	Ala	Ala	Asp	Leu	Leu	
			20					25						30		
ggc	ccc	gac	ggg	ctg	ggc	ctg	tgg	cgg	ccg	gac	gtg	cag	gag	ccg	acc	144
Gly	Pro	Asp	Gly	Leu	Gly	Leu	Trp	Arg	Pro	Asp	Val	Gln	Glu	Pro	Thr	
			35				40						45			
gac	gac	cgc	gcg	gcg	gag	ctg	ctc	gcc	gcg	ctc	tcc	cgg	gcc	gcc	gac	192
Asp	Asp	Arg	Ala	Ala	Glu	Leu	Leu	Ala	Ala	Leu	Ser	Arg	Ala	Ala	Asp	
			50				55					60				
ccg	gac	ctg	gcg	ctg	cgc	cag	ctc	cac	cgc	atc	gtc	gag	gcg	gag	cgc	240
Pro	Asp	Leu	Ala	Leu	Arg	Gln	Leu	His	Arg	Ile	Val	Glu	Ala	Glu	Arg	
			65			70				75					80	
cgg	gcc	gcc	ggc	ccg	gcg	gcc	acc	ggc	tcg	gcg	ctg	gtg	gag	gcg	ctc	288
Arg	Ala	Ala	Gly	Pro	Ala	Ala	Thr	Gly	Ser	Ala	Leu	Val	Glu	Ala	Leu	
				85					90					95		
gcg	gac	gac	ccg	ggg	ctg	cgc	cgc	cgg	ctg	atc	gcc	gtc	ctc	ggc	gcc	336
Ala	Asp	Asp	Pro	Gly	Leu	Arg	Arg	Arg	Leu	Ile	Ala	Val	Leu	Gly	Ala	
			100					105					110			
tcc	tcg	gcg	ctg	ggc	gac	cac	ctg	gtc	gcc	aac	ccc	gac	cag	tgg	ccg	384
Ser	Ser	Ala	Leu	Gly	Asp	His	Leu	Val	Ala	Asn	Pro	Asp	Gln	Trp	Pro	
			115				120						125			
gcc	ctg	cgg	acc	gcc	ccg	gac	ggg	ctc	gcg	ccg	acc	gcg	gag	ggc	cgg	432
Ala	Leu	Arg	Thr	Ala	Pro	Asp	Gly	Leu	Ala	Pro	Thr	Ala	Glu	Gly	Arg	
			130				135					140				
ctc	gac	ctg	tcc	ggc	gac	ggg	cag	ccg	gtc	gcg	gtg	ctg	cgc	aag	gcg	480
Leu	Asp	Leu	Ser	Gly	Asp	Gly	Gln	Pro	Val	Ala	Val	Leu	Arg	Lys	Ala	
					150					155					160	
tac	cgg	ctg	gcg	ctg	ctg	cgg	atc	gcg	gcg	gcc	gac	ctg	acc	ggc	gac	528
Tyr	Arg	Leu	Ala	Leu	Leu	Arg	Ile	Ala	Ala	Ala	Asp	Leu	Thr	Gly	Asp	
				165					170					175		
cgg	ggc	ctg	gag	cag	acg	atg	gcc	gcg	ctc	tcc	gcg	ttg	gcc	gac	gcg	576
Arg	Gly	Leu	Glu	Gln	Thr	Met	Ala	Ala	Leu	Ser	Ala	Leu	Ala	Asp	Ala	
			180					185						190		
acc	ctg	gcg	gcg	gcg	tac	gag	atc	gcc	gtc	ggc	gag	ctg	ccg	gag	ggc	624
Thr	Leu	Ala	Ala	Ala	Tyr	Glu	Ile	Ala	Val	Gly	Glu	Leu	Pro	Glu	Gly	
			195				200					205				
acg	ccc	cgg	ccc	cgg	ctc	gcc	gtc	gtg	gcg	atg	ggc	aag	tgc	ggc	ggc	672
Thr	Pro	Arg	Pro	Arg	Leu	Ala	Val	Val	Ala	Met	Gly	Lys	Cys	Gly	Gly	
			210				215					220				

gac gag ctg aac tac gtc tcc gac gtc gac gtg atc ttc gtg gcc gcc	720
Asp Glu Leu Asn Tyr Val Ser Asp Val Asp Val Ile Phe Val Ala Ala	
225 230 235 240	
gag gac gac gac ctc gcc gcg gcc acc acg gtc gcc acc cgg ctg atc	768
Glu Asp Asp Asp Leu Ala Ala Ala Thr Thr Val Ala Thr Arg Leu Ile	
245 250 255	
cac gtc tgc ggg ctg gtc gcc tgg ccg gtc gac gcc gcc ctg cgg ccc	816
His Val Cys Gly Leu Val Ala Trp Pro Val Asp Ala Ala Leu Arg Pro	
260 265 270	
gag ggc aat cgt ggc ccg ctg gtg cgc acc ctg gcc agc cac ctc gcc	864
Glu Gly Asn Arg Gly Pro Leu Val Arg Thr Leu Ala Ser His Leu Ala	
275 280 285	
tac tac cgg cgc tgg gcg cgg acg tgg gag ttc cag gcg ctg ctc aag	912
Tyr Tyr Arg Arg Trp Ala Arg Thr Trp Glu Phe Gln Ala Leu Leu Lys	
290 295 300	
gcc cgg ccg gcg gcc ggc gac ctg acc ctg gcc cgg gag tgg atc gac	960
Ala Arg Pro Ala Ala Gly Asp Leu Thr Leu Gly Arg Glu Trp Ile Asp	
305 310 315 320	
cag ctc gcc ccg ctc gtg tgg cgg gcc gcc gag cgc ccc gag gcg gtc	1008
Gln Leu Ala Pro Leu Val Trp Arg Ala Ala Glu Arg Pro Glu Ala Val	
325 330 335	
gag gac gtc cgc gcc atg cgg cgg aag atc atc gac aac gtc ccg ccg	1056
Glu Asp Val Arg Ala Met Arg Arg Lys Ile Ile Asp Asn Val Pro Pro	
340 345 350	
aag gag ttg gag cgc gag atc aag cgc gcc ccg gcc ggg ctg cgc gac	1104
Lys Glu Leu Glu Arg Glu Ile Lys Arg Gly Pro Gly Gly Leu Arg Asp	
355 360 365	
atc gag ttc gcc gtc cag ctg ctg caa ctg gtg cac gcc cgg gcc gac	1152
Ile Glu Phe Ala Val Gln Leu Leu Gln Leu Val His Gly Arg Gly Asp	
370 375 380	
gag tcg ctg cgg acg ccc gcc acc gtc ccg gcg ctg cgc gcg ctc gtc	1200
Glu Ser Leu Arg Thr Pro Gly Thr Val Pro Ala Leu Arg Ala Leu Val	
385 390 395 400	
gcc gcc gcc tac gtc gcc cgg gcc gac ggg gag gcg ctg ctg cgc gcc	1248
Ala Gly Gly Tyr Val Gly Arg Ala Asp Gly Glu Ala Leu Leu Arg Gly	
405 410 415	
tac cgc ttc ctg cgc gcc gtc gag cac cgc ctc cag ctc cag ggg ctg	1296
Tyr Arg Phe Leu Arg Gly Val Glu His Arg Leu Gln Leu Gln Gly Leu	
420 425 430	
cgc cgc acc cac acc gtg ccg acc gag ccg gcc gcg ctg cgc tgg ttg	1344
Arg Arg Thr His Thr Val Pro Thr Glu Pro Ala Ala Leu Arg Trp Leu	
435 440 445	
gcc gcc gcg ctg gcc tac gcg gcc acg ccg gcc cgc agc gcc gtc gag	1392

Ala Ala Ala Leu Gly Tyr Ala Ala Thr Pro Gly Arg Ser Ala Val Glu	
450	455 460
gag ttc cgc gcc gag tgg gtc acc cac gcc acc gag gta cgc cgg ctg	1440
Glu Phe Arg Ala Glu Trp Val Thr His Ala Thr Glu Val Arg Arg Leu	
465	470 475 480
cac gcc aag ctg ctc tac cgg ccg ctg ctg gag tcg gtg gcc cgg gtg	1488
His Ala Lys Leu Leu Tyr Arg Pro Leu Leu Glu Ser Val Ala Arg Val	
	485 490 495
ccg gcc gac ggg ctg cgg ctg acc ccg gag gcg gcc cgg cac cgg ctg	1536
Pro Ala Asp Gly Leu Arg Leu Thr Pro Glu Ala Ala Arg His Arg Leu	
	500 505 510
gag atc ctc ggc ttc gcc gac ccc gcc ggg gcg ctg cgg cac ctc cag	1584
Glu Ile Leu Gly Phe Ala Asp Pro Ala Gly Ala Leu Arg His Leu Gln	
	515 520 525
gcc ctc acc ggc ggg gtg agc cgc acg gcg gcc atc cag cgc acc ctg	1632
Ala Leu Thr Gly Gly Val Ser Arg Thr Ala Ala Ile Gln Arg Thr Leu	
	530 535 540
ctg ccg gtg ctg ctc agc gag ttc gcc gac gcc ccc gag ccg gac cgc	1680
Leu Pro Val Leu Leu Ser Glu Phe Ala Asp Ala Pro Glu Pro Asp Arg	
	545 550 555 560
ggc ctg ctc aac tac cgg cag gtc tcc gac aag ctc ggc agc acg ccc	1728
Gly Leu Leu Asn Tyr Arg Gln Val Ser Asp Lys Leu Gly Ser Thr Pro	
	565 570 575
tgg tac ctg cgc ctg ctg cgc gac tcc ggg ccg gtg gcc cgc cgg ctg	1776
Trp Tyr Leu Arg Leu Leu Arg Asp Ser Gly Pro Val Ala Arg Arg Leu	
	580 585 590
gcc cgg gtg ctc tcc tcc tcc cgc tac gcc gcc gac ctg ctg gcc cgc	1824
Ala Arg Val Leu Ser Ser Ser Arg Tyr Ala Ala Asp Leu Leu Ala Arg	
	595 600 605
gag ccg gag gcg ctg cgg atg ctg gcc gag gag agc gag ttg acc ccc	1872
Glu Pro Glu Ala Leu Arg Met Leu Ala Glu Glu Ser Glu Leu Thr Pro	
	610 615 620
cgg ccg agc ggg gtg ctc tgc gag ggc ttc gcc gcc gcc gca gcc cgg	1920
Arg Pro Ser Gly Val Leu Cys Glu Gly Phe Ala Ala Ala Ala Ala Arg	
	625 630 635 640
cac gcc gac ccc gtc gaa gcc acc cgg gcg atc cgc gcg ctg cgc cgc	1968
His Ala Asp Pro Val Glu Ala Thr Arg Ala Ile Arg Ala Leu Arg Arg	
	645 650 655
cgg gag ctg gtc cgc atc gcc tgc gcg gac ctg ttg agc cgg gcc ggc	2016
Arg Glu Leu Val Arg Ile Ala Cys Ala Asp Leu Leu Ser Arg Ala Gly	
	660 665 670
tcg ctg gcc ccg tcg ccg ccc cgg ccc gac ggc ggg cgg gcc gcg ctc	2064
Ser Leu Ala Pro Ser Pro Pro Arg Pro Asp Gly Gly Arg Ala Ala Leu	
	675 680 685

ggt ctc gcc gac gtc gcc gcc gtg ggc acg gcg ctg gcc gac gtc acc	2112
Gly Leu Ala Asp Val Ala Ala Val Gly Thr Ala Leu Ala Asp Val Thr	
690 695 700	
gac gcc acc ctg gcc gcg gcg ctg cgg gcc gcc cgg gcc gcc cag ccg	2160
Asp Ala Thr Leu Ala Ala Ala Leu Arg Ala Ala Arg Ala Ala Gln Pro	
705 710 715 720	
ccc atg ccg ggg ctg cgc ttc gcc gtg atc ggc atg ggc cgc ctg ggc	2208
Pro Met Pro Gly Leu Arg Phe Ala Val Ile Gly Met Gly Arg Leu Gly	
725 730 735	
ggg tac gag tcg aac tac ctc tcc gac gcc gac gtg ctc ttc gtc tac	2256
Gly Tyr Glu Ser Asn Tyr Leu Ser Asp Ala Asp Val Leu Phe Val Tyr	
740 745 750	
gac ccc ccg ccc ggc gcc ggc gag agc gcg gcc ggc gcg gcg agc gcc	2304
Asp Pro Pro Pro Gly Ala Gly Glu Ser Ala Ala Gly Ala Ala Ser Ala	
755 760 765	
gcc gcc cac ggg atc gcc gag gag ttg cgt cgg ctg ctc ggc atg ccc	2352
Ala Ala His Gly Ile Ala Glu Glu Leu Arg Arg Leu Leu Gly Met Pro	
770 775 780	
gcg ccc gac ccg ccg ctg ggc gtg gac gcc gac ctg cgt ccc gag ggc	2400
Ala Pro Asp Pro Pro Leu Gly Val Asp Ala Asp Leu Arg Pro Glu Gly	
785 790 795 800	
cgg cag ggt ccg ctc gtg cgc agc ctc gcc gcg tac gcg cag tac tac	2448
Arg Gln Gly Pro Leu Val Arg Ser Leu Ala Ala Tyr Ala Gln Tyr Tyr	
805 810 815	
gcc cgc tgg tcg aag gtg tgg gag gcg cag gcg ctg ctg cgt gcc cgg	2496
Ala Arg Trp Ser Lys Val Trp Glu Ala Gln Ala Leu Leu Arg Ala Arg	
820 825 830	
ttc gtc tgc ggc gac gcc gac ctc ggc gcg gag ttc gag gcg atg gtc	2544
Phe Val Cys Gly Asp Ala Asp Leu Gly Ala Glu Phe Glu Ala Met Val	
835 840 845	
gac ccg gtc cgc tac ccg gcc gac ggg ttg acc cgc gag cag gtg gtg	2592
Asp Pro Val Arg Tyr Pro Ala Asp Gly Leu Thr Arg Glu Gln Val Val	
850 855 860	
gag atc cgg cgg atc aag gcg cgg gtg gag cac gag cgg ctg ccc cgg	2640
Glu Ile Arg Arg Ile Lys Ala Arg Val Glu His Glu Arg Leu Pro Arg	
865 870 875 880	
ggc gcc gac ccg gcc acc cac acc aag ctc ggg cgg ggc ggc ctc gcc	2688
Gly Ala Asp Pro Ala Thr His Thr Lys Leu Gly Arg Gly Gly Leu Ala	
885 890 895	
gac gtc gag tgg gcg gtg caa ctg ctc cag ctc cgg cac gcc ggg acg	2736
Asp Val Glu Trp Ala Val Gln Leu Leu Gln Leu Arg His Ala Gly Thr	
900 905 910	
gtc ccg cgg ctg cgc ggc acg cgt acg ctc gac gcc ctc gcg gcg gcc	2784

Val	Pro	Arg	Leu	Arg	Gly	Thr	Arg	Thr	Leu	Asp	Ala	Leu	Ala	Ala	Ala		
		915					920					925					
cgg	gac	gcg	ggg	ctg	gtc	gac	ccg	acg	gac	gcc	acc	gag	atg	gcg	gcc	2832	
Arg	Asp	Ala	Gly	Leu	Val	Asp	Pro	Thr	Asp	Ala	Thr	Glu	Met	Ala	Ala		
		930				935					940						
ggc	tgg	acc	ctg	gcc	gcg	cag	gtc	cgc	aac	gcg	ctg	atg	ctg	gtc	cgc	2880	
Gly	Trp	Thr	Leu	Ala	Ala	Gln	Val	Arg	Asn	Ala	Leu	Met	Leu	Val	Arg		
		945				950				955					960		
ggc	cgg	gcc	ggc	gac	cag	ttg	ccc	cgg	cac	ggc	gtc	gag	ttg	gcc	ggg	2928	
Gly	Arg	Ala	Gly	Asp	Gln	Leu	Pro	Arg	His	Gly	Val	Glu	Leu	Ala	Gly		
				965					970						975		
gtg	gtc	cgg	ctg	ctc	ggc	cgg	gac	gat	ccc	ggc	gag	ttc	ctc	gac	gag	2976	
Val	Val	Arg	Leu	Leu	Gly	Arg	Asp	Asp	Pro	Gly	Glu	Phe	Leu	Asp	Glu		
			980					985						990			
tac	ctg	cgc	acc	ggc	cgc	cgc	tcc	cgc	gcg	gcg	atg	gag	cgg	gtc	ctc	3024	
Tyr	Leu	Arg	Thr	Gly	Arg	Arg	Ser	Arg	Ala	Ala	Met	Glu	Arg	Val	Leu		
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gac	gcc	tga														3033	
Asp	Ala	*															
		1010															

<210> 82  
 <211> 296  
 <212> PRT  
 <213> Bacteria

<400> 82																	
Val	Ile	Leu	Val	Ala	Leu	Ala	Lys	Ile	Arg	Glu	Val	Pro	Leu	Thr	Gly		
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Ala	Asp	Ala	Gly	Pro	Tyr	Gly	Val	Thr	Val	Gly	Pro	Asp	Gly	Ala	Leu		
			20					25					30				
Trp	Leu	Thr	Leu	Val	His	Ala	Gly	Ala	Val	Ala	Arg	Val	Gly	Ala	Asp		
		35					40					45					
Gly	Asp	Leu	Arg	Thr	Trp	Gln	Val	Ala	Ala	Asp	Ser	Arg	Pro	Leu	Ile		
	50					55					60						
Val	Thr	Pro	Gly	Pro	Asp	Gly	Ala	Leu	Trp	Phe	Thr	Arg	Ser	Gly	Asp		
	65				70					75				80			
Asp	Arg	Ile	Gly	Arg	Ile	Thr	Thr	Asp	Gly	Glu	Gln	Ser	Ala	Val	Ala		
				85				90						95			
Leu	Pro	Pro	Gly	Ser	Gly	Pro	Cys	Gly	Ile	Ala	Ala	Gly	Pro	Asp	Gly		
			100					105					110				
Ala	Leu	Trp	Tyr	Ala	Ala	Met	Thr	Ala	Asp	Ala	Val	Gly	Arg	Val	Thr		
		115					120					125					
Thr	Asp	Gly	Lys	Val	Thr	Gln	Phe	Pro	Leu	Pro	Val	Ser	Gly	Gly	Phe		
	130					135					140						
Ala	Ser	Met	Val	Ala	Ala	Gly	Pro	Asp	Glu	Ala	Val	Trp	Phe	Thr	Leu		
	145				150					155					160		
Asn	Gln	Ala	Asn	Ala	Val	Gly	Arg	Ile	Gly	Thr	Asp	Gly	Ala	Val	Ala		
			165					170						175			
Leu	His	Pro	Leu	Pro	Thr	Glu	Gly	Ala	Ala	Pro	Val	Gly	Ile	Thr	Ala		
			180					185						190			



Gly	Ala	Asp	Gly	Ala	Leu	Trp	Phe	Val	Glu	Ile	Gly	Ala	Gly	Gln	Leu
	195						200					205			
Gly	Arg	Ile	Thr	Pro	Asp	Gly	Arg	Ile	Asp	Glu	Tyr	Pro	Leu	Pro	Asp
	210					215					220				
Arg	Ala	Ala	Arg	Pro	His	Ala	Ile	Val	Ala	Asp	Pro	Ala	Gly	Gly	Cys
225					230					235					240
Trp	Phe	Thr	Glu	Trp	Gly	Gly	Asn	Arg	Ile	Gly	His	Val	Ala	Pro	Asp
				245					250					255	
Gly	Thr	Ile	Val	Thr	His	Asp	Leu	Pro	Thr	Pro	Ala	Ala	Glu	Pro	His
			260					265					270		
Gly	Ile	Thr	Val	Ala	Pro	Asp	Gly	Thr	Val	Trp	Ala	Ala	Leu	Glu	Thr
	275						280					285			
Gly	Ala	Leu	Ala	His	Leu	Thr	Pro								
	290					295									

<210> 83  
 <211> 705  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(705)

<400> 83																
gtg	cga	cac	gac	gga	acg	gcc	ggg	gag	cac	cgg	cac	gac	agg	acg	gcg	48
Val	Arg	His	Asp	Gly	Thr	Ala	Gly	Glu	His	Arg	His	Asp	Arg	Thr	Ala	
1				5				10					15			
gcg ccg gtg gac gac cat tgg cgg cac ccg gac gtg gac gag gag acc															96	
Ala	Pro	Val	Asp	Asp	His	Trp	Arg	His	Pro	Asp	Val	Asp	Glu	Glu	Thr	
			20				25					30				
gct cgg tac tgg gag gag ctc tac ggg cgg cgc gac cgg tac tgg agc															144	
Ala	Arg	Tyr	Trp	Glu	Glu	Leu	Tyr	Gly	Arg	Arg	Asp	Arg	Tyr	Trp	Ser	
		35				40					45					
ggg cgg gcg aac ccg atc ctg gtc gac gtc gcc ggg ccg ctg ccg gcc															192	
Gly	Arg	Ala	Asn	Pro	Ile	Leu	Val	Asp	Val	Ala	Gly	Pro	Leu	Pro	Ala	
	50					55				60						
ggc acc gcg ctg gac ctc ggc tgc ggc gag ggc ggc gac gcg atc tgg															240	
Gly	Thr	Ala	Leu	Asp	Leu	Gly	Cys	Gly	Glu	Gly	Gly	Asp	Ala	Ile	Trp	
	65				70				75					80		
ctg gcc ggg cgg ggc tgg cgg gtg acg gcg gtg gac gtc gcc gag acc															288	
Leu	Ala	Gly	Arg	Gly	Trp	Arg	Val	Thr	Ala	Val	Asp	Val	Ala	Glu	Thr	
				85				90					95			
gcc ctc gac cgg gcg tcc gca gcg gcg gcc gag gcc ggg gtg gcg tcc															336	
Ala	Leu	Asp	Arg	Ala	Ser	Ala	Ala	Ala	Glu	Ala	Gly	Val	Ala	Ser		
			100					105				110				
cgc atc gag ttc cgc cgg cac gac ctc acc cgg acc ttc ccg ccg ggc															384	
Arg	Ile	Glu	Phe	Arg	Arg	His	Asp	Leu	Thr	Arg	Thr	Phe	Pro	Pro	Gly	
	115						120					125				

gag ttc gac ctg gtc tcc gcg cag ttc ctc cag tcg ccg ctg gag ttc	432
Glu Phe Asp Leu Val Ser Ala Gln Phe Leu Gln Ser Pro Leu Glu Phe	
130 135 140	
ccc cgg gga gag gtg ctg cgc tcg gcg gcc cgg gcc gtg gcc ccc ggc	480
Pro Arg Gly Glu Val Leu Arg Ser Ala Ala Arg Ala Val Ala Pro Gly	
145 150 155 160	
ggc cgg ctg ctc gtc gtc gag cac ggc gag gtc ccg ccg tgg gga cgg	528
Gly Arg Leu Leu Val Val Glu His Gly Glu Val Pro Pro Trp Gly Arg	
165 170 175	
cac gcg cac ccg gac gtg cgc ttc ccc acc ccg cag gag acc ctc gcc	576
His Ala His Pro Asp Val Arg Phe Pro Thr Pro Gln Glu Thr Leu Ala	
180 185 190	
gag ctg gac ctc gac ccg gac cgg tgg ctc acc gag cgg ctc gac gcc	624
Glu Leu Asp Leu Asp Pro Asp Arg Trp Leu Thr Glu Arg Leu Asp Ala	
195 200 205	
ccg cgc cgg cag gcc acc ggc ccg gac ggc cat acc ggg acc ctc gtc	672
Pro Arg Arg Gln Ala Thr Gly Pro Asp Gly His Thr Gly Thr Leu Val	
210 215 220	
gac cac gtg gtg ctg gtc cgc cgc cgc ccg tag	705
Asp His Val Val Leu Val Arg Arg Arg Pro *	
225 230	

<210> 84  
 <211> 234  
 <212> PRT  
 <213> Bacteria

<400> 84  
 Val Arg His Asp Gly Thr Ala Gly Glu His Arg His Asp Arg Thr Ala  
 1 5 10 15  
 Ala Pro Val Asp Asp His Trp Arg His Pro Asp Val Asp Glu Glu Thr  
 20 25 30  
 Ala Arg Tyr Trp Glu Glu Leu Tyr Gly Arg Arg Asp Arg Tyr Trp Ser  
 35 40 45  
 Gly Arg Ala Asn Pro Ile Leu Val Asp Val Ala Gly Pro Leu Pro Ala  
 50 55 60  
 Gly Thr Ala Leu Asp Leu Gly Cys Gly Glu Gly Gly Asp Ala Ile Trp  
 65 70 75 80  
 Leu Ala Gly Arg Gly Trp Arg Val Thr Ala Val Asp Val Ala Glu Thr  
 85 90 95  
 Ala Leu Asp Arg Ala Ser Ala Ala Ala Glu Ala Gly Val Ala Ser  
 100 105 110  
 Arg Ile Glu Phe Arg Arg His Asp Leu Thr Arg Thr Phe Pro Pro Gly  
 115 120 125  
 Glu Phe Asp Leu Val Ser Ala Gln Phe Leu Gln Ser Pro Leu Glu Phe  
 130 135 140  
 Pro Arg Gly Glu Val Leu Arg Ser Ala Ala Arg Ala Val Ala Pro Gly  
 145 150 155 160  
 Gly Arg Leu Leu Val Val Glu His Gly Glu Val Pro Pro Trp Gly Arg  
 165 170 175  
 His Ala His Pro Asp Val Arg Phe Pro Thr Pro Gln Glu Thr Leu Ala



tcc gac gcc gac ggg cgg gcg cgg cga cgg cag gtc gcg cgg ctc ggg	528
Ser Asp Ala Asp Gly Arg Ala Arg Arg Arg Gln Val Ala Arg Leu Gly	
165 170 175	
ctg gcg gtc gcc ggg gcg ctg ctg gcc tcg gcg gcg agc ccg gtg gcg	576
Leu Ala Val Ala Gly Ala Leu Leu Ala Ser Ala Ala Ser Pro Val Ala	
180 185 190	
ggc ctc ttc gtc ggc ctg gcc ggc gcg gcg ctg ctg ctc acc cgc cgg	624
Gly Leu Phe Val Gly Leu Ala Gly Ala Ala Leu Leu Leu Thr Arg Arg	
195 200 205	
tac gcc gac ggc ctg gcg ctc ggc gtc gcc gcc gcg ctg ccg ctc ggg	672
Tyr Ala Asp Gly Leu Ala Leu Gly Val Ala Ala Leu Pro Leu Gly	
210 215 220	
gcg acc gcg ctg ctc ttc ggc gac ggc ggc tgg atg aac atc agc cgc	720
Ala Thr Ala Leu Leu Phe Gly Asp Gly Gly Trp Met Asn Ile Ser Arg	
225 230 235 240	
acc gac acg ctg cgc gcc gtg ctg acc agc ctg ctg gtc gcc gcg ctg	768
Thr Asp Thr Leu Arg Ala Val Leu Thr Ser Leu Leu Val Ala Ala Leu	
245 250 255	
gtg gcg tac cgg ccg gtg cgg gtg ggc gcg ctg ctc tcg gcg gcc ggg	816
Val Ala Tyr Arg Pro Val Arg Val Gly Ala Leu Leu Ser Ala Ala Gly	
260 265 270	
gtg ctg gcg gcg gcg ctg gtg cac acc ccg gtc ggg ctg aac gcc acc	864
Val Leu Ala Ala Ala Leu Val His Thr Pro Val Gly Leu Asn Ala Thr	
275 280 285	
cgg ctg gcg gtc atg ttc ggc ctg ccg ctg ctg gcc gcc gcc gcc cgc	912
Arg Leu Ala Val Met Phe Gly Leu Pro Leu Leu Ala Ala Ala Arg	
290 295 300	
ccc ccg gtc ggg ctg gcg cgg tgg tgg gcc cga cgc ggg cgg ggc gcg	960
Pro Pro Val Gly Leu Ala Arg Trp Trp Ala Arg Arg Gly Arg Gly Ala	
305 310 315 320	
gcg cgg ggc ggg gtg ggc ggc cgg gac gcg gcg cag ggg cgg agc aag	1008
Ala Arg Gly Gly Val Gly Gly Arg Asp Ala Ala Gln Gly Arg Ser Lys	
325 330 335	
gtc cgg ggc cgc gtg gcg ctg gcc acg ctg ctg gcg gcc ggc tgc tgg	1056
Val Arg Gly Arg Val Ala Leu Ala Thr Leu Leu Ala Ala Gly Cys Trp	
340 345 350	
tgg cag ccg ccg gtg ccc ccc gcc gac ctg cgc agc gtc gac gac ccg	1104
Trp Gln Pro Pro Val Pro Pro Ala Asp Leu Arg Ser Val Asp Asp Pro	
355 360 365	
acc ggc cgg gcc gcg tac ttg cgc cgc tgc ggg agt tcc tcg acg ggc	1152
Thr Gly Arg Ala Ala Tyr Leu Arg Arg Cys Gly Ser Ser Ser Thr Gly	
370 375 380	
agc ggc tca ccg gcc ggg tcg agg tgc cgc cga ccc gca act act ggg	1200

Ser Gly Ser Pro Ala Gly Ser Arg Cys Arg Arg Pro Ala Thr Thr Gly  
 385 390 395 400

agg cgg cgc ggc tgg gcg agg tgc cgc tgg ccc ggg gct ggc tgc ggc 1248  
 Arg Arg Arg Gly Trp Ala Arg Cys Arg Trp Pro Gly Ala Gly Cys Gly  
 405 410 415

agg ccg aca tcg acc gga acc ccc tct tct tca cca ccg tcc cgg gcg 1296  
 Arg Pro Thr Ser Thr Gly Thr Pro Ser Ser Ser Pro Pro Ser Arg Ala  
 420 425 430

cgg ccg gca ccg ggg tgc cgc tga 1320  
 Arg Pro Ala Pro Gly Cys Arg \*

<210> 86  
 <211> 439  
 <212> PRT  
 <213> Bacteria

<400> 86  
 Val Gly Met Arg Arg Ser Arg Val Val Ala Val Ala Ala Ala Ser Ala  
 1 5 10 15  
 Val Leu Leu Gly Val Thr Tyr Leu Ala Leu Pro Pro Thr Gly Ser Asp  
 20 25 30  
 Leu Ala Ala Gln Val Ala Arg Ala Asp Phe Phe Ala Ala His Gly Leu  
 35 40 45  
 Ala Pro Val Asp Leu Arg Trp Tyr Gly Gly Val Gln Gln Phe Gly Tyr  
 50 55 60  
 Ser Leu Val Ser Gln Pro Val Met Ala Leu Leu Gly Val Arg Val Thr  
 65 70 75 80  
 Gly Val Leu Ala Leu Val Ala Ala Ala Thr Ala Phe Ala Ala Leu Leu  
 85 90 95  
 Val Arg Thr Gly Val Pro Arg Pro Leu Leu Gly Ser Leu Val Gly Val  
 100 105 110  
 Val Thr Ile Ala Gly Asn Leu Val Ser Gly Arg Val Thr Tyr Gly Leu  
 115 120 125  
 Gly Val Ala Phe Gly Leu Gly Ala Leu Leu Ala Leu Thr Leu Pro Arg  
 130 135 140  
 Gly Pro Ala Ala Arg Ala Ala Asp Ser Asp Pro Ala Ala Pro Ala Asp  
 145 150 155 160  
 Ser Asp Ala Asp Gly Arg Ala Arg Arg Arg Gln Val Ala Arg Leu Gly  
 165 170 175  
 Leu Ala Val Ala Gly Ala Leu Leu Ala Ser Ala Ala Ser Pro Val Ala  
 180 185 190  
 Gly Leu Phe Val Gly Leu Ala Gly Ala Ala Leu Leu Leu Thr Arg Arg  
 195 200 205  
 Tyr Ala Asp Gly Leu Ala Leu Gly Val Ala Ala Ala Leu Pro Leu Gly  
 210 215 220  
 Ala Thr Ala Leu Leu Phe Gly Asp Gly Gly Trp Met Asn Ile Ser Arg  
 225 230 235 240  
 Thr Asp Thr Leu Arg Ala Val Leu Thr Ser Leu Leu Val Ala Ala Leu  
 245 250 255  
 Val Ala Tyr Arg Pro Val Arg Val Gly Ala Leu Leu Ser Ala Ala Gly  
 260 265 270  
 Val Leu Ala Ala Ala Leu Val His Thr Pro Val Gly Leu Asn Ala Thr  
 275 280 285

Arg Leu Ala Val Met Phe Gly Leu Pro Leu Leu Ala Ala Ala Ala Arg  
 290 295 300  
 Pro Pro Val Gly Leu Ala Arg Trp Trp Ala Arg Arg Gly Arg Gly Ala  
 305 310 315 320  
 Ala Arg Gly Gly Val Gly Gly Arg Asp Ala Ala Gln Gly Arg Ser Lys  
 325 330 335  
 Val Arg Gly Arg Val Ala Leu Ala Thr Leu Leu Ala Ala Gly Cys Trp  
 340 345 350  
 Trp Gln Pro Pro Val Pro Pro Ala Asp Leu Arg Ser Val Asp Asp Pro  
 355 360 365  
 Thr Gly Arg Ala Ala Tyr Leu Arg Arg Cys Gly Ser Ser Ser Thr Gly  
 370 375 380  
 Ser Gly Ser Pro Ala Gly Ser Arg Cys Arg Arg Pro Ala Thr Thr Gly  
 385 390 395 400  
 Arg Arg Arg Gly Trp Ala Arg Cys Arg Trp Pro Gly Ala Gly Cys Gly  
 405 410 415  
 Arg Pro Thr Ser Thr Gly Thr Pro Ser Ser Ser Pro Pro Ser Arg Ala  
 420 425 430  
 Arg Pro Ala Pro Gly Cys Arg  
 435

<210> 87

<211> 1431

<212> DNA

<213> Bacteria

<220>

<221> CDS

<222> (1)...(1431)

<400> 87

atg tcc ggc gtg cct cac cac ctc gcg cgc tgg atc ggc ctg gcc ggc 48  
 Met Ser Gly Val Pro His His Leu Ala Arg Trp Ile Gly Leu Ala Gly  
 1 5 10 15

tcg acg ctg ctc gcc gtg gcc gcg ttc ctc ggc gga gcg ctg ccc gac 96  
 Ser Thr Leu Leu Ala Val Ala Ala Phe Leu Gly Gly Ala Leu Pro Asp  
 20 25 30

ggc gat ttg cgc ccc acc ccg ctc agc atc tgg cag ggc ccg cac ggc 144  
 Gly Asp Leu Arg Pro Thr Pro Leu Ser Ile Trp Gln Gly Pro His Gly  
 35 40 45

ccg ttg atc atc gcc acc tgg gcg gtc ggc acg ggc ctg atg gcg tac 192  
 Pro Leu Ile Ile Ala Thr Trp Ala Val Gly Thr Gly Leu Met Ala Tyr  
 50 55 60

gcc tgg tgg gcg ctg cgc gac cgg gtg ccg tcg acc cgc tgg gcc gtg 240  
 Ala Trp Trp Ala Leu Arg Asp Arg Val Pro Ser Thr Arg Trp Ala Val  
 65 70 75 80

gtc acc gcc ggg ctc tgg ctg ctg ccg ctg ctg gtc gcg ccg ccg ctg 288  
 Val Thr Ala Gly Leu Trp Leu Leu Pro Leu Leu Val Ala Pro Pro Leu  
 85 90 95

ggc agc cga gac gtc tac gcg tac gcc tgc cag ggc gcc agc tac tcc 336  
 Gly Ser Arg Asp Val Tyr Ala Tyr Ala Cys Gln Gly Ala Ser Tyr Ser



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gcc gcg ccg ttc ggc tgg cac ggc gat ccg ctg ccg gtc acc cgg ggc 1056
Ala Ala Pro Phe Gly Trp His Gly Asp Pro Leu Pro Val Thr Arg Gly
      340      345      350

atc ggg atg gcc gtg ctc gcg ctg gtg ctg atc tgg ctg tgg tgg cgg 1104
Ile Gly Met Ala Val Leu Ala Leu Val Leu Ile Trp Leu Trp Trp Arg
      355      360      365

gcc cgc acc cgg gag ccg ctg tgg cac gcc ggc ctg gcg ctg gcc gcc 1152
Ala Arg Thr Arg Glu Pro Leu Trp His Ala Gly Leu Ala Leu Ala Ala
      370      375      380

acg gtc gcg ctc gcc ccg ctg ttc cac ccc tgg tac tgg acc tgg ccg 1200
Thr Val Ala Leu Ala Pro Leu Phe His Pro Trp Tyr Trp Thr Trp Pro
385      390      395      400

ctg gcc gtg ctc gcg gcc acg tcg cgg cgc acc ggc tgg ttc gcg ctc 1248
Leu Ala Val Leu Ala Ala Thr Ser Arg Arg Thr Gly Trp Phe Ala Leu
      405      410      415

gtc gcg gtg ctc tcg gcg ttc ctg gtc ctc gcg gac ggc acc ggg ctg 1296
Val Ala Val Leu Ser Ala Phe Leu Val Leu Ala Asp Gly Thr Gly Leu
      420      425      430

gcc cgg tac agc aag acg gtc ggc gcc ccg ctg atg acg ctg ttg gtg 1344
Ala Arg Tyr Ser Lys Thr Val Gly Ala Pro Leu Met Thr Leu Leu Val
      435      440      445

atg gtg gtg gcc gtc cgc ttg gta cgg tcg gct tgg gcg gcc cgc cgg 1392
Met Val Val Ala Val Arg Leu Val Arg Ser Ala Trp Ala Ala Arg Arg
      450      455      460

tcg gct cgg gcg gcc cgc cgg ccg gcc gcc gtg aac tga 1431
Ser Ala Arg Ala Ala Arg Pro Ala Ala Val Asn *
465      470      475

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<210> 88  
 <211> 476  
 <212> PRT  
 <213> Bacteria

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<400> 88
Met Ser Gly Val Pro His His Leu Ala Arg Trp Ile Gly Leu Ala Gly
  1      5      10      15
Ser Thr Leu Leu Ala Val Ala Ala Phe Leu Gly Gly Ala Leu Pro Asp
      20      25      30
Gly Asp Leu Arg Pro Thr Pro Leu Ser Ile Trp Gln Gly Pro His Gly
      35      40      45
Pro Leu Ile Ile Ala Thr Trp Ala Val Gly Thr Gly Leu Met Ala Tyr
      50      55      60
Ala Trp Trp Ala Leu Arg Asp Arg Val Pro Ser Thr Arg Trp Ala Val
      65      70      75      80
Val Thr Ala Gly Leu Trp Leu Leu Pro Leu Leu Val Ala Pro Pro Leu
      85      90      95
Gly Ser Arg Asp Val Tyr Ala Tyr Ala Cys Gln Gly Ala Ser Tyr Ser
      100      105      110
Ala Gly Ile Asn Pro Tyr Glu Gln Gly Val Ser Ala Leu Pro Cys Pro

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      115              120              125
Trp Leu Asp Thr Ile Ser Tyr Ile Trp Arg Asp Thr Ser Ala Pro Tyr
      130              135              140
Gly Pro Leu Phe Leu Leu Ile Ala Gly Ala Val Val Glu Ala Thr Gly
145              150              155              160
Ser Leu Thr Gly Ser Ile Val Leu Phe Arg Leu Leu Ala Val Ala Gly
      165              170              175
Val Gly Leu Thr Ala Ala Cys Leu Pro Pro Leu Ala Arg Arg Cys Gly
      180              185              190
Val Pro Ala Gly Arg Ala Val Trp Leu Ala Leu Gly Ser Pro Leu Ile
      195              200              205
Gly Val His Leu Ile Ser Gly Ala His Asn Asp Ala Leu Met Val Gly
      210              215              220
Leu Leu Val Ala Gly Leu Ala Met Val Val Ala Arg Pro Gly Arg Pro
225              230              235              240
Gly Pro Leu Leu Ala Gly Gly Ala Leu Leu Gly Leu Ala Gly Ala Val
      245              250              255
Lys Val Thr Ala Leu Val Val Val Pro Phe Ala Ala Leu Ala Ala Ile
      260              265              270
Val Gly Ala Tyr Ser Ile Arg Ala Leu Ile Arg Asp Gly Gly Trp Val
      275              280              285
Val Gly Gly Ala Leu Ala Ala Val Val Gly Ala Thr Leu Ala Ser Gly
      290              295              300
Leu Gly Phe Gly Trp Val Thr Gly Leu Glu Gln Gly Gly Leu Val Ile
305              310              315              320
Ala Trp Thr Ser Pro Pro Thr Ala Val Gly Gln Thr Val Ala Tyr Leu
      325              330              335
Ala Ala Pro Phe Gly Trp His Gly Asp Pro Leu Pro Val Thr Arg Gly
      340              345              350
Ile Gly Met Ala Val Leu Ala Leu Val Leu Ile Trp Leu Trp Trp Arg
      355              360              365
Ala Arg Thr Arg Glu Pro Leu Trp His Ala Gly Leu Ala Leu Ala Ala
      370              375              380
Thr Val Ala Leu Ala Pro Leu Phe His Pro Trp Tyr Trp Thr Trp Pro
385              390              395              400
Leu Ala Val Leu Ala Ala Thr Ser Arg Arg Thr Gly Trp Phe Ala Leu
      405              410              415
Val Ala Val Leu Ser Ala Phe Leu Val Leu Ala Asp Gly Thr Gly Leu
      420              425              430
Ala Arg Tyr Ser Lys Thr Val Gly Ala Pro Leu Met Thr Leu Leu Val
      435              440              445
Met Val Val Ala Val Arg Leu Val Arg Ser Ala Trp Ala Ala Arg Arg
      450              455              460
Ser Ala Arg Ala Ala Arg Arg Pro Ala Ala Val Asn
465              470              475

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<210> 89  
 <211> 1509  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(1509)

<400> 89  
 gtg acc aca ccc ggc tcc ccg tcg acc tcg ccc gac gtc tcg ccg tcg 48

Val	Thr	Thr	Pro	Gly	Ser	Pro	Ser	Thr	Ser	Pro	Asp	Val	Ser	Pro	Ser	
1				5					10					15		
ccg	gat	gcc	gcc	cgg	ctc	gcc	cgg	tac	gcg	ggc	ctg	ggc	ggg	gcg	gtg	96
Pro	Asp	Ala	Ala	Arg	Leu	Ala	Arg	Tyr	Ala	Gly	Leu	Gly	Gly	Ala	Val	
			20					25					30			
ctg	ttg	gcc	gtc	gcc	ggc	tgg	cgg	ggc	ggg	gcg	ctg	ccg	tcg	acc	ccg	144
Leu	Leu	Ala	Val	Ala	Gly	Trp	Arg	Gly	Gly	Ala	Leu	Pro	Ser	Thr	Pro	
		35					40					45				
ctg	gac	gtc	ccc	ccg	ggg	gac	cgt	tgg	ctg	tcg	gac	ggg	ggg	ccg	ctg	192
Leu	Asp	Val	Pro	Pro	Gly	Asp	Arg	Trp	Leu	Ser	Asp	Gly	Gly	Pro	Leu	
	50					55					60					
acg	ctg	ggg	gtc	tgg	ctg	gtc	ggc	acg	gcc	ctg	ctg	gtc	ggc	gcc	tgg	240
Thr	Leu	Gly	Val	Trp	Leu	Val	Gly	Thr	Ala	Leu	Leu	Val	Gly	Ala	Trp	
65					70				75						80	
tgg	gcg	ctg	cgc	cgg	ggc	gcg	ccg	tcc	acg	cgg	tgg	gcg	tac	ctg	acc	288
Trp	Ala	Leu	Arg	Arg	Gly	Ala	Pro	Ser	Thr	Arg	Trp	Ala	Tyr	Leu	Thr	
			85						90					95		
gcc	ggg	ctg	tgg	gcg	ctg	ccg	ctg	ctg	gtc	acc	ccg	ccg	ctg	ggc	agc	336
Ala	Gly	Leu	Trp	Ala	Leu	Pro	Leu	Leu	Val	Thr	Pro	Pro	Leu	Gly	Ser	
			100					105					110			
cgg	gac	gtc	tac	tcc	tac	gcc	tgc	cag	ggc	tgg	gcg	tac	gcg	cac	ggc	384
Arg	Asp	Val	Tyr	Ser	Tyr	Ala	Cys	Gln	Gly	Trp	Ala	Tyr	Ala	His	Gly	
		115					120					125				
gtc	gac	ccg	tac	gcg	acc	ggg	gtg	gcc	gag	gcc	ggc	tgc	ccc	tgg	gtg	432
Val	Asp	Pro	Tyr	Ala	Thr	Gly	Val	Ala	Glu	Ala	Gly	Cys	Pro	Trp	Val	
	130					135					140					
gag	tcg	gtc	gcg	ccg	atc	tgg	cgg	gac	acg	ccc	gcc	ccg	tac	ggg	ccg	480
Glu	Ser	Val	Ala	Pro	Ile	Trp	Arg	Asp	Thr	Pro	Ala	Pro	Tyr	Gly	Pro	
145					150					155					160	
ttc	ttc	gtg	ctg	ctc	gcc	gcg	ctc	gcg	gtg	acc	ctc	ggc	ggc	ggc	ctg	528
Phe	Phe	Val	Leu	Leu	Ala	Ala	Leu	Ala	Val	Thr	Leu	Gly	Gly	Gly	Leu	
			165						170					175		
gtg	ggc	gct	gtc	gtg	gcg	ttc	cgc	ctg	ctc	gcg	gtc	gcc	ggg	gtg	ttg	576
Val	Gly	Ala	Val	Val	Ala	Phe	Arg	Leu	Leu	Ala	Val	Ala	Gly	Val	Leu	
			180					185					190			
ctg	gcc	gcc	ctc	tgc	ctg	gtg	ggc	ctg	gcc	cgc	gcc	gcg	ggc	gtg	ccc	624
Leu	Ala	Ala	Leu	Cys	Leu	Val	Gly	Leu	Ala	Arg	Ala	Ala	Gly	Val	Pro	
			195				200					205				
acc	cgc	agg	gcg	gcc	tgg	ctg	gcg	ctg	gcc	tgc	ccg	ctg	gtc	ggg	gtc	672
Thr	Arg	Arg	Ala	Ala	Trp	Leu	Ala	Leu	Ala	Cys	Pro	Leu	Val	Gly	Val	
	210					215					220					
cac	ctg	gtg	gcc	ggc	gcg	cac	aac	gac	gcg	gtg	atg	ctc	ggc	ctg	ctg	720
His	Leu	Val	Ala	Gly	Ala	His	Asn	Asp	Ala	Val	Met	Leu	Gly	Leu	Leu	
225					230					235					240	

ctg ctg ggc ctg ctg gtg ctg gtg cgc ggg ccc ggc aag ccg aag ccg	768
Leu Leu Gly Leu Leu Val Leu Val Arg Gly Pro Gly Lys Pro Lys Pro	
245 250 255	
ctg ttg gtg gcc ggg gcc ctg ctc ggg ctg gcg gtg acg gtg aag gcc	816
Leu Leu Val Ala Gly Ala Leu Leu Gly Leu Ala Val Thr Val Lys Ala	
260 265 270	
acc gcc gtg gtg gtg ctt ccc ttc gcg gcg ctg gcc gcg gtg ctg ggc	864
Thr Ala Val Val Val Leu Pro Phe Ala Ala Leu Ala Ala Val Leu Gly	
275 280 285	
cgc tac acc gtg cgg gcg ctg ctg cgc gac gcc ggc tgg ctg gcc ggc	912
Arg Tyr Thr Val Arg Ala Leu Leu Arg Asp Ala Gly Trp Leu Ala Gly	
290 295 300	
ggg acg ctc ggc gcg gtg ggg gtc acc tcg ctg ctg tcc ggc ctc gga	960
Gly Thr Leu Gly Ala Val Gly Val Thr Ser Leu Leu Ser Gly Leu Gly	
305 310 315 320	
ctc ggc tgg ata cgc ggg ctg acc cgc agc ggg gac tcc gag cag tgg	1008
Leu Gly Trp Ile Arg Gly Leu Thr Arg Ser Gly Asp Ser Glu Gln Trp	
325 330 335	
acg tcg ccc ccg acg gcg gtg ggc ttc gtc gtc gac tac gcg ggc gag	1056
Thr Ser Pro Pro Thr Ala Val Gly Phe Val Val Asp Tyr Ala Gly Glu	
340 345 350	
ctc gcc ggg cgg gac ccg ggc gcg gtg ccg gcg acc cgc gcg gcg gcg	1104
Leu Ala Gly Arg Asp Pro Gly Ala Val Pro Ala Thr Arg Ala Ala Ala	
355 360 365	
ctg ctg ctg ctc gcc gtg ctc gtg gcg gcg ctg tgg tgg cgg gcc tgg	1152
Leu Leu Leu Leu Ala Val Leu Val Ala Ala Leu Trp Trp Arg Ala Trp	
370 375 380	
tcg ggg ctg cgc cgg ctg aac gac gtc cgg cag cgg gtg gcc cgc ctg	1200
Ser Gly Leu Arg Arg Leu Asn Asp Val Arg Gln Arg Val Ala Arg Leu	
385 390 395 400	
gac gcc gcc cgc ccc cgg gtg acc ctg ctc ggc gcg ggg ctg gcg ctg	1248
Asp Ala Ala Arg Pro Arg Val Thr Leu Leu Gly Ala Gly Leu Ala Leu	
405 410 415	
gcc gcc acg gtc ctc ctc gcc ccg gtc ttc cac ccc tgg tac gcc acc	1296
Ala Ala Thr Val Leu Leu Ala Pro Val Phe His Pro Trp Tyr Ala Thr	
420 425 430	
tgg ccg ctg gcc ctg ctc gcg gtc gcc gcg acg cgg acc acc tgg ttc	1344
Trp Pro Leu Ala Leu Leu Ala Val Ala Ala Thr Arg Thr Thr Trp Phe	
435 440 445	
gtg gcg ccc tgc gcg gcg gcg gcc ttc ctc acc ctg ccc gac ggc acc	1392
Val Ala Pro Cys Ala Ala Ala Phe Leu Thr Leu Pro Asp Gly Thr	
450 455 460	
aac ctg gcc cgg ttc acc aag gcc ccg ggc gcg atc gcg atg acc gcg	1440





	85	90	95	
gcc ggg ttc acc ccg ccg gcc ggc gcg gcg tgg cag ccg ctc atc ccg				336
Ala Gly Phe Thr Pro Pro Ala Gly Ala Ala Trp Gln Arg Leu Ile Pro				
	100	105	110	
ccg gac ccg gag gaa ctc gtc tgc cac aac gac gtg gcc ccg tgg aac				384
Pro Asp Arg Glu Glu Leu Val Cys His Asn Asp Val Ala Pro Trp Asn				
	115	120	125	
ctg atc agg gcg gac ccg ggc tgg gtg ctg atc gac tgg gac tgc gcg				432
Leu Ile Arg Ala Asp Arg Gly Trp Val Leu Ile Asp Trp Asp Cys Ala				
	130	135	140	
gcg ccg ggc tcc ccg ctc tgg gac ctc gcg tac gcc gcg cag agc atg				480
Ala Pro Gly Ser Arg Leu Trp Asp Leu Ala Tyr Ala Ala Gln Ser Met				
	145	150	155	160
gcc ggc ctg cgc ccg gac ccg ccg gtg gcc gag tcg gcg gcc ccg ctg				528
Ala Gly Leu Arg Pro Asp Arg Pro Val Ala Glu Ser Ala Ala Arg Leu				
	165	170	175	
cgc gcc ttc gcc gac ggc tac ccg ctg gac gag gcg tcc cgc ccg gcc				576
Arg Ala Phe Ala Asp Gly Tyr Arg Leu Asp Glu Ala Ser Arg Pro Ala				
	180	185	190	
ctg gcc gcc atg ctg ggt cgc cgc gcc ccg gcc atg tac gac ctg ttg				624
Leu Ala Ala Met Leu Gly Arg Arg Ala Arg Ala Met Tyr Asp Leu Leu				
	195	200	205	
cgc gag ggc gcg gaa cag ccg cgc gag ccg tgg gcc ccg atc tgg acc				672
Arg Glu Gly Ala Glu Gln Arg Arg Glu Pro Trp Ala Arg Ile Trp Thr				
	210	215	220	
gag gac ggc ccg tac tgg ctg gcc acc gcc gaa cac ctc gac gcc cac				720
Glu Asp Gly Pro Tyr Trp Leu Ala Thr Ala Glu His Leu Asp Ala His				
	225	230	235	240
acc gag gca tgg gag atc gcc ctg cgc tga				750
Thr Glu Ala Trp Glu Ile Ala Leu Arg *				
	245			

<210> 92

<211> 249

<212> PRT

<213> Bacteria

<400> 92

Met Ser Thr Ala Glu Glu Ser Leu Pro Gly Asn Ala Thr Thr Gly Val				
1 5 10 15				
Val Arg Val Gly Asp Thr Val Arg Arg Pro Val Gly Pro Trp Ser Asp				
20 25 30				
Val Val Asp Ala Leu Leu Glu His Leu His Ala Val Gly Phe Ala Gly				
35 40 45				
Ala Pro Arg Pro Leu Gly Arg Asp Ala Gln Gly Arg Gln Val Leu Glu				
50 55 60				
Tyr Val Pro Gly Glu Val Gly Glu Ala Ser Gly Thr Tyr Pro Val Ala				

65					70					75				80	
Asp	Leu	Phe	Ala	Ile	Gly	Arg	Met	Leu	Ala	Glu	Leu	His	Glu	Ala	Leu
				85						90				95	
Ala	Gly	Phe	Thr	Pro	Pro	Ala	Gly	Ala	Ala	Trp	Gln	Arg	Leu	Ile	Pro
				100						105				110	
Pro	Asp	Arg	Glu	Glu	Leu	Val	Cys	His	Asn	Asp	Val	Ala	Pro	Trp	Asn
				115						120				125	
Leu	Ile	Arg	Ala	Asp	Arg	Gly	Trp	Val	Leu	Ile	Asp	Trp	Asp	Cys	Ala
				130						135				140	
Ala	Pro	Gly	Ser	Arg	Leu	Trp	Asp	Leu	Ala	Tyr	Ala	Ala	Gln	Ser	Met
				145						150				155	
Ala	Gly	Leu	Arg	Pro	Asp	Arg	Pro	Val	Ala	Glu	Ser	Ala	Ala	Arg	Leu
				165						170				175	
Arg	Ala	Phe	Ala	Asp	Gly	Tyr	Arg	Leu	Asp	Glu	Ala	Ser	Arg	Pro	Ala
				180						185				190	
Leu	Ala	Ala	Met	Leu	Gly	Arg	Arg	Ala	Arg	Ala	Met	Tyr	Asp	Leu	Leu
				195						200				205	
Arg	Glu	Gly	Ala	Glu	Gln	Arg	Arg	Glu	Pro	Trp	Ala	Arg	Ile	Trp	Thr
				210						215				220	
Glu	Asp	Gly	Pro	Tyr	Trp	Leu	Ala	Thr	Ala	Glu	His	Leu	Asp	Ala	His
				225						230				235	
Thr	Glu	Ala	Trp	Glu	Ile	Ala	Leu	Arg							
				245											

<210> 93  
 <211> 1315  
 <212> DNA  
 <213> Bacteria

<400> 93  
 catcctccct cgcctaaagg cgggggagtc cgaccctcgc ggggtgggggt tcctggttca 60  
 ccgcagaccg cacggaagga ggctccttcgt gtctgacgtc cgctccgcag gcgtttttcg 120  
 tctcggccag cccggccgcg acggtgatgt tcttggtctgc gttgacgtcc cggtcattgcc 180  
 ggggtgccga actcggacac gtccagtggc gtgtgcccag ggagagtgtg gcgagcaggt 240  
 gccgcacgc cgagcaggtc ttcgacgacg ggtaccagcg gtccaccacc gcgaggggtgc 300  
 ggccgtcgcg gtgcgccttg taggtgagca ggggtgcggaa ctcgggccag cgggtacgcg 360  
 agatcgcttt ggccagggag tggttgcgga ccatgttcgc caccggccagg tcctccacgg 420  
 cgatggcggc gaaccggcgc accagggcgg tggactgctg gtggaggaag tcccggcggg 480  
 cgtcgcgcac ctgcgaatgc gtcggggcga ccattcgctt ggctttggcg cggttggcgg 540  
 agcccttctg tcggcgggcc attatccgct gataccgctt gaggcggcgt tcccgccggt 600  
 ccatgtgctt cgggtggggg atgcgttcgc cgggtggacag caccgcgaag tcggtcaggc 660  
 cgaggtccac gccaccgcc tcgccggtgg gtccgggtgc ggcgggtgtg tcgacgtcga 720  
 cggcgaaggt cacgaaccag cggccgtccg ggtcacgcga caccgtcacc atcgtcggat 780  
 ccaaccccg cggatccacg ttcggcaacg accacacgaa ccgcagcacc ccgggtgtct 840  
 ttcccaacga caggttcccg ctgcggaggc ggaacgccga ccgggtgtaa ctggcggaact 900  
 ggcgcccggt tcgggacttg tagcgcggtt accggggccc cttggcgaag aaggcgggtca 960  
 tggcggtgtg ctggtgccgc aggggtctgt gcaacggcac cgacgacacc tcaccagat 1020  
 acgccaggtc gggctgcttc ttcattctcc tcaacgccc atcggtctcc gcgtaggagg 1080  
 tggatctccg ttcggtgtgc cagcgggcgt gacggggcgg gacggtgcgg ttccagacga 1140  
 cacgtacaca cccgaacgtg cggttcagca ccgcgcgctg ctccgggggtc gggtagcccc 1200  
 gacacctgta cggcgtccgc acaggaccag ccctaccaga aaggacagtc gtggctgaca 1260  
 acgcatccgc cgttcgtccc cgccctgaag gacgtggcat cctggcggtg atccg 1315

<210> 94  
 <211> 1263  
 <212> DNA  
 <213> Bacteria

<220>  
 <221> CDS  
 <222> (1)...(1263)

<400> 94

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Val Leu Asp Met Thr Gln Val Asp Gly Ser Pro Leu Pro Thr Leu Glu	
1 5 10 15	
agg caa gtg atc acc gtg cgt gtg ctg ttc gcc agt ctc gga acc cat	96
Arg Gln Val Ile Thr Val Arg Val Leu Phe Ala Ser Leu Gly Thr His	
20 25 30	
ggc cac acc tac ccc ctg ctg cca ctg gcc acg gcc gcc cgt gcg gcg	144
Gly His Thr Tyr Pro Leu Leu Pro Leu Ala Thr Ala Arg Ala Ala	
35 40 45	
ggc cac gag gtc acc ttc gcc acc ggc gag ggc ttc gcg ggc acc ctg	192
Gly His Glu Val Thr Phe Ala Thr Gly Glu Gly Phe Ala Gly Thr Leu	
50 55 60	
cgg aag ctg ggc ttc gag ccg gtc gcg acc ggg atg ccg gtc ttc gac	240
Arg Lys Leu Gly Phe Glu Pro Val Ala Thr Gly Met Pro Val Phe Asp	
65 70 75 80	
ggg ttc ctg gcg gcg ctg cgg atc cgc ttc gac acc gac agc ccc gag	288
Gly Phe Leu Ala Ala Leu Arg Ile Arg Phe Asp Thr Asp Ser Pro Glu	
85 90 95	
ggg ctg acc ccc gag cag ctc agt gag ctg ccg cag atc gtg ttc ggg	336
Gly Leu Thr Pro Glu Gln Leu Ser Glu Leu Pro Gln Ile Val Phe Gly	
100 105 110	
cgg gtc atc ccg cag cgc gtc ttc gac gag ctc cag ccg gtg atc gaa	384
Arg Val Ile Pro Gln Arg Val Phe Asp Glu Leu Gln Pro Val Ile Glu	
115 120 125	
cgg ttg cga ccc gac ctc gtg gtg cag gag atc agc aac tac ggc gcc	432
Arg Leu Arg Pro Asp Leu Val Val Gln Glu Ile Ser Asn Tyr Gly Ala	
130 135 140	
ggc ctg gcc gcc ctg aag gcg ggc atc ccg acc atc tgc cac ggg gtc	480
Gly Leu Ala Ala Leu Lys Ala Gly Ile Pro Thr Ile Cys His Gly Val	
145 150 155 160	
ggc cgg gac acg ccg gac gac ctg acc cgg tcc atc gag gag gag gtg	528
Gly Arg Asp Thr Pro Asp Asp Leu Thr Arg Ser Ile Glu Glu Glu Val	
165 170 175	
cgg ggg ctg gcc cag cgg ctc ggc ctc gac ctg ccg ccc ggg cgc atc	576
Arg Gly Leu Ala Gln Arg Leu Gly Leu Asp Leu Pro Pro Gly Arg Ile	
180 185 190	
gac ggc ttc ggc aac ccc ttc atc gac atc ttc ccg ccg tcg ctg cag	624
Asp Gly Phe Gly Asn Pro Phe Ile Asp Ile Phe Pro Pro Ser Leu Gln	
195 200 205	
gag ccg gag ttc cgg gcc cgc ccg cgg cgc cac gag ctg cgc ccg gtg	672



Glu	Pro	Glu	Phe	Arg	Ala	Arg	Pro	Arg	Arg	His	Glu	Leu	Arg	Pro	Val		
210						215					220						
ccc	ttc	gcc	gag	cag	ggg	gac	ctc	ccg	gcc	tgg	ctg	tcc	tcg	cgc	gac	720	
Pro	Phe	Ala	Glu	Gln	Gly	Asp	Leu	Pro	Ala	Trp	Leu	Ser	Ser	Arg	Asp		
225					230					235					240		
acg	gcc	cgc	ccg	ctg	gtc	tac	ctg	acg	ctc	ggc	acg	tcc	agc	ggc	ggc	768	
Thr	Ala	Arg	Pro	Leu	Val	Tyr	Leu	Thr	Leu	Gly	Thr	Ser	Ser	Gly	Gly		
				245						250				255			
acc	gtc	gag	gtg	ctg	cgg	gcg	gcg	atc	gac	ggg	ctc	gcc	ggc	ctc	gac	816	
Thr	Val	Glu	Val	Leu	Arg	Ala	Ala	Ile	Asp	Gly	Leu	Ala	Gly	Leu	Asp		
			260					265					270				
gcc	gac	gtc	ctg	gtc	gcc	agc	ggc	ccg	tcc	ctc	gac	gtc	agc	gga	ctg	864	
Ala	Asp	Val	Leu	Val	Ala	Ser	Gly	Pro	Ser	Leu	Asp	Val	Ser	Gly	Leu		
		275					280						285				
ggc	gag	gtg	ccg	gca	aac	gta	cgg	ctc	gag	tcg	tgg	gtg	ccg	cag	gcg	912	
Gly	Glu	Val	Pro	Ala	Asn	Val	Arg	Leu	Glu	Ser	Trp	Val	Pro	Gln	Ala		
	290					295					300						
gcc	ctg	ctg	ccc	cac	gtc	gac	ctg	gtg	gtg	cac	cac	ggg	ggc	agc	ggc	960	
Ala	Leu	Leu	Pro	His	Val	Asp	Leu	Val	Val	His	His	Gly	Gly	Ser	Gly		
305					310					315					320		
act	acg	ctc	ggc	gca	ctg	ggc	gcc	ggc	gtg	ccg	cag	ctg	tcc	ttc	ccg	1008	
Thr	Thr	Leu	Gly	Ala	Leu	Gly	Ala	Gly	Val	Pro	Gln	Leu	Ser	Phe	Pro		
				325					330					335			
tgg	gcg	ggg	gac	tcg	ttc	gcc	aac	gcg	cag	gcg	gtg	gcg	cag	gcc	ggc	1056	
Trp	Ala	Gly	Asp	Ser	Phe	Ala	Asn	Ala	Gln	Ala	Val	Ala	Gln	Ala	Gly		
			340					345					350				
gcc	ggg	gac	cac	ctg	ctg	ccc	gac	aac	atc	agc	ccc	gac	tcg	gtg	tcg	1104	
Ala	Gly	Asp	His	Leu	Leu	Pro	Asp	Asn	Ile	Ser	Pro	Asp	Ser	Val	Ser		
		355					360					365					
ggc	gcc	gcg	aag	cgc	ctg	ttg	gcc	gag	gag	agc	tac	cgg	gcc	ggg	gcg	1152	
Gly	Ala	Ala	Lys	Arg	Leu	Leu	Ala	Glu	Glu	Ser	Tyr	Arg	Ala	Gly	Ala		
	370					375				380							
cgg	gcc	gtg	gcg	gcc	gag	atc	gcg	gcc	atg	ccg	ggc	ccc	gac	gag	gtc	1200	
Arg	Ala	Val	Ala	Ala	Glu	Ile	Ala	Ala	Met	Pro	Gly	Pro	Asp	Glu	Val		
385					390					395					400		
gtc	cgc	ctg	ctg	ccg	ggc	ttc	gcc	tcc	agg	agc	gcg	ggc	tga	ccg	gcg	1248	
Val	Arg	Leu	Leu	Pro	Gly	Phe	Ala	Ser	Arg	Ser	Ala	Gly	*	Pro	Ala		
				405					410						415		
cta	cgt	ctg	ccg	tag												1263	
Leu	Arg	Leu	Pro	*													

<210> 95  
<211> 419

<212> PRT  
<213> Bacteria

<400> 95

Val	Leu	Asp	Met	Thr	Gln	Val	Asp	Gly	Ser	Pro	Leu	Pro	Thr	Leu	Glu
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Arg	Gln	Val	Ile	Thr	Val	Arg	Val	Leu	Phe	Ala	Ser	Leu	Gly	Thr	His
			20					25					30		
Gly	His	Thr	Tyr	Pro	Leu	Leu	Pro	Leu	Ala	Thr	Ala	Ala	Arg	Ala	Ala
		35					40					45			
Gly	His	Glu	Val	Thr	Phe	Ala	Thr	Gly	Glu	Gly	Phe	Ala	Gly	Thr	Leu
	50					55					60				
Arg	Lys	Leu	Gly	Phe	Glu	Pro	Val	Ala	Thr	Gly	Met	Pro	Val	Phe	Asp
65					70					75					80
Gly	Phe	Leu	Ala	Ala	Leu	Arg	Ile	Arg	Phe	Asp	Thr	Asp	Ser	Pro	Glu
				85					90					95	
Gly	Leu	Thr	Pro	Glu	Gln	Leu	Ser	Glu	Leu	Pro	Gln	Ile	Val	Phe	Gly
			100					105					110		
Arg	Val	Ile	Pro	Gln	Arg	Val	Phe	Asp	Glu	Leu	Gln	Pro	Val	Ile	Glu
		115					120					125			
Arg	Leu	Arg	Pro	Asp	Leu	Val	Val	Gln	Glu	Ile	Ser	Asn	Tyr	Gly	Ala
	130					135						140			
Gly	Leu	Ala	Ala	Leu	Lys	Ala	Gly	Ile	Pro	Thr	Ile	Cys	His	Gly	Val
145					150					155					160
Gly	Arg	Asp	Thr	Pro	Asp	Asp	Leu	Thr	Arg	Ser	Ile	Glu	Glu	Glu	Val
				165					170					175	
Arg	Gly	Leu	Ala	Gln	Arg	Leu	Gly	Leu	Asp	Leu	Pro	Pro	Gly	Arg	Ile
			180					185					190		
Asp	Gly	Phe	Gly	Asn	Pro	Phe	Ile	Asp	Ile	Phe	Pro	Pro	Ser	Leu	Gln
	195						200					205			
Glu	Pro	Glu	Phe	Arg	Ala	Arg	Pro	Arg	Arg	His	Glu	Leu	Arg	Pro	Val
	210					215						220			
Pro	Phe	Ala	Glu	Gln	Gly	Asp	Leu	Pro	Ala	Trp	Leu	Ser	Ser	Arg	Asp
225					230					235					240
Thr	Ala	Arg	Pro	Leu	Val	Tyr	Leu	Thr	Leu	Gly	Thr	Ser	Ser	Gly	Gly
				245					250					255	
Thr	Val	Glu	Val	Leu	Arg	Ala	Ala	Ile	Asp	Gly	Leu	Ala	Gly	Leu	Asp
			260					265					270		
Ala	Asp	Val	Leu	Val	Ala	Ser	Gly	Pro	Ser	Leu	Asp	Val	Ser	Gly	Leu
	275						280					285			
Gly	Glu	Val	Pro	Ala	Asn	Val	Arg	Leu	Glu	Ser	Trp	Val	Pro	Gln	Ala
	290				295						300				
Ala	Leu	Leu	Pro	His	Val	Asp	Leu	Val	Val	His	His	Gly	Gly	Ser	Gly
305					310					315					320
Thr	Thr	Leu	Gly	Ala	Leu	Gly	Ala	Gly	Val	Pro	Gln	Leu	Ser	Phe	Pro
				325					330					335	
Trp	Ala	Gly	Asp	Ser	Phe	Ala	Asn	Ala	Gln	Ala	Val	Ala	Gln	Ala	Gly
			340					345					350		
Ala	Gly	Asp	His	Leu	Leu	Pro	Asp	Asn	Ile	Ser	Pro	Asp	Ser	Val	Ser
	355						360					365			
Gly	Ala	Ala	Lys	Arg	Leu	Leu	Ala	Glu	Glu	Ser	Tyr	Arg	Ala	Gly	Ala
	370					375					380				
Arg	Ala	Val	Ala	Ala	Glu	Ile	Ala	Ala	Met	Pro	Gly	Pro	Asp	Glu	Val
385					390					395					400
Val	Arg	Leu	Leu	Pro	Gly	Phe	Ala	Ser	Arg	Ser	Ala	Gly	Pro	Ala	Leu
				405					410					415	
Arg	Leu	Pro													